
U.S. PUBLIC HEALTH SERVICE
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U. S. PUBLIC HEALTH

HOSPITALS AND

BASIC DRUGS

U. S. Public Health Service Hospitals and Clinics

–1953–

FEDERAL SECURITY AGENCY
PUBLIC HEALTH SERVICE
Bureau of Medical Services
Division of Hospitals

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TABLE OF CONTENTS

FOREWORD

The adoption of a system of basic drugs for the Division of Hospitals is expected to stimulate medical and dental officers to become and remain familiar with good pharmacologic practice, to insure that medical and dental officers moving from one station to another will find at least the familiar solid core of basic drugs at their new stations, to encourage therapeutic simplicity, and to maintain reasonable control over the inventories of our pharmacies without denying any medical or dental officer the opportunity of convincing his fellow clinicians that a "nonbasic" drug is essential for the welfare of his patients.

The basic drugs presented in the following pages are thought of as the group from which each station shall choose the items to be regularly stocked in its pharmacy. Within such regulations as each medical officer in charge may establish, we would think of this group of drugs as being freely available to any chief of service who desires to have them stocked in the pharmacy.

Nonbasic drugs may be stocked at each station only with the written approval of the station pharmacy committee. This requirement does not apply to the procurement of a nonbasic drug for an individual patient in an emergency. This function is left in the hands of the medical officer in charge and may, at his discretion, be delegated to chiefs of service or to junior officers.

Each station has been requested, as part of its monthly pharmacy report, to report the nonbasic drugs which its pharmacy committee has approved for station use. Nonbasic drugs which prove to have a high rate of acceptance by the stations will eventually be added to the list of basic drugs in future revisions.

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INTRODUCTION

Drug therapy is a broad and complex field. The multiplicity of available drugs and drug preparations, and the rapidity of developments in this field, make it difficult for the physician and dentist to keep up to date and to be discriminative. Such compendia as New and Nonofficial Remedies, Useful Drugs, Reports of the Council on Pharmacy and Chemistry of the American Medical Association, and Accepted Dental Remedies of the American Dental Association, serve to help the physician and dentist in improving and keeping current their drug armamentarium. The majority of practitioners, however, feel that further simplification would be desirable, especially with respect to those drugs which tend to duplicate one another's effects or which offer chemical or pharmacologic variations of questionable advantage.

Basic Drugs—U. S. Public Health Service Hospitals and Clinics has been developed in an effort to meet this need. This basic listing is not the end but the beginning, the point of departure, in drug therapy. The development of this handbook has been a cooperative Service effort which has had the following purposes and goals:

1. To provide the patient with the best possible drug therapy.
2. To provide the physician and dentist with carefully selected agents of proved effectiveness, which will be a basis for flexible drug therapy.
3. To provide a standard of comparison for the evaluation of new therapeutic agents.
4. To provide the physician, dentist, pharmacist, and nurse with a ready reference on the essential pharmacology of the basic drugs.
5. To provide for simplification of all drug therapy record keeping.

In the selection of basic drugs, an attempt has been made to sort out the smallest number of the best, simplest, and safest medicines currently needed in the ordinary prevention, diagnosis, and treatment of illness. Only rarely was the task one of sorting the good from the bad or indifferent. Usually it involved trying to choose the best of several good medications. The criteria utilized in the selection of drugs were:

1. The primary consideration is the therapeutic efficacy of the drug. Within this criterion, preference is given to U. S. Pharmacopeia, The National Formulary, New and Nonofficial Remedies, and Accepted Dental Remedies items.
2. Unnecessary duplication is avoided.
3. Drugs with secret composition are not considered.
4. Mixtures are included only when they provide substantial advantage over the individual components.

Many vehicles, wetting and emulsifying agents, oils, coloring agents, and similar items used in the practice of pharmacy, are not included in this listing. Such routinely used agents are of course to be stocked in Service pharmacies as needed.

Along with the standardization of drugs, it is recommended that meaningful drug terminology be adopted to the greatest possible extent. It is not safe practice to use synonyms, numbers, common names, trade names, and pseudonyms in prescription writing or in clinical records. The drugs in the handbook are there are usually referred to by their official English titles, if they are official in

dies, American Dental Association. In some instances, an official drug such as Neostigmine (trade name "Prostigmin") is produced by one manufacturer and is obtainable only under the trade name. Such drugs are referred to by the official or the N. N. R. or A. D. A. name and the trade name follows in parentheses, and dosage forms are expressed in terms of the trade name. If other trade names for the same drug appear subsequently, or if the drug becomes available under the official or N. N. R. name, then the official or N. N. R. name alone will be used.

We recommend the adoption of the metric system as rapidly and as completely as possible.

The use of code numbers, letters, symbols, or other nonidentifying abbreviations in any pharmaceutical terminology, including prescription writing, doctors' orders, clinical notes, or in the operation of the pharmacy, is not acceptable practice and should not be followed in hospitals and clinics of the Public Health Service.

It is emphasized again that the basic drugs presented in the following pages are thought of as a group from which each station shall choose the items to be regularly stocked in its pharmacy. Within such regulations as each medical officer in charge may establish, we would think of this group of drugs as being freely available to any chief of service who desires to have them stocked. Nonbasic drugs may be stocked at each station only with the written approval of the station pharmacy committee. This requirement does not apply to the procurement of nonbasic drugs for an individual patient in an emergency. This function is left in the hands of the medical officer in charge and may, at his discretion, be delegated to chiefs of service, or to junior officers. The Form, PHS-1089 (HSP), which is used to request approval of the pharmacy committee for nonbasic drugs, is reproduced on page 4, following the discussion of the Pharmacy Committee.

The pharmacy committee will usually consist of the chiefs of the medical, surgical, dental, nursing, and pharmacy services and, in the larger institutions, the clinical director and chiefs of other clinical services, especially the EENT and dermatological services. The clinical director, or if there is no such officer at the station, the chief of the medical service, will serve as chairman with the pharmacist acting as the recorder and secretary.

Meetings

Meetings should be held regularly at least six times a year, and preferably monthly.

Minutes and Records

It is recommended that records be prepared by the pharmacist and that the permanent record of the committee's activities be kept in the pharmacy. Copies of minutes and records that indicate positive actions of the committee on other than routine actions should be prepared in triplicate, i. e., the committee's record, a copy for the medical officer in charge, and a copy for transmittal to the Chief of the Division of Hospitals, Washington 25, D. C., Attention: Pharmacy Branch.

Functions

The functions of the committee should be to:

(1) Prepare and formulate current information on drug therapy for the guidance of the staff.

(2) Review periodically the stock status of drugs with special reference to pharmaceutical specialties in order to avoid the development of surplus stock of usable drugs.

(3) Consider periodically the additions and deletions of items from New and Nonofficial Remedies (N. N. R.) and Accepted Dental Remedies (A. D. R.) as summarized by the monthly Hospital Division Circular Memorandums on the subject.

(4) Serve as an advisory group to the pharmacist regarding the therapeutic agents to be stocked in the pharmacy.

(5) Serve as an advisory group to the pharmacy department regarding therapeutic agents to be stocked as ward medications.

(6) Consider other pharmaceutical or related matters referred by the Medical Officer in Charge or by Headquarters.

Basic Drug List

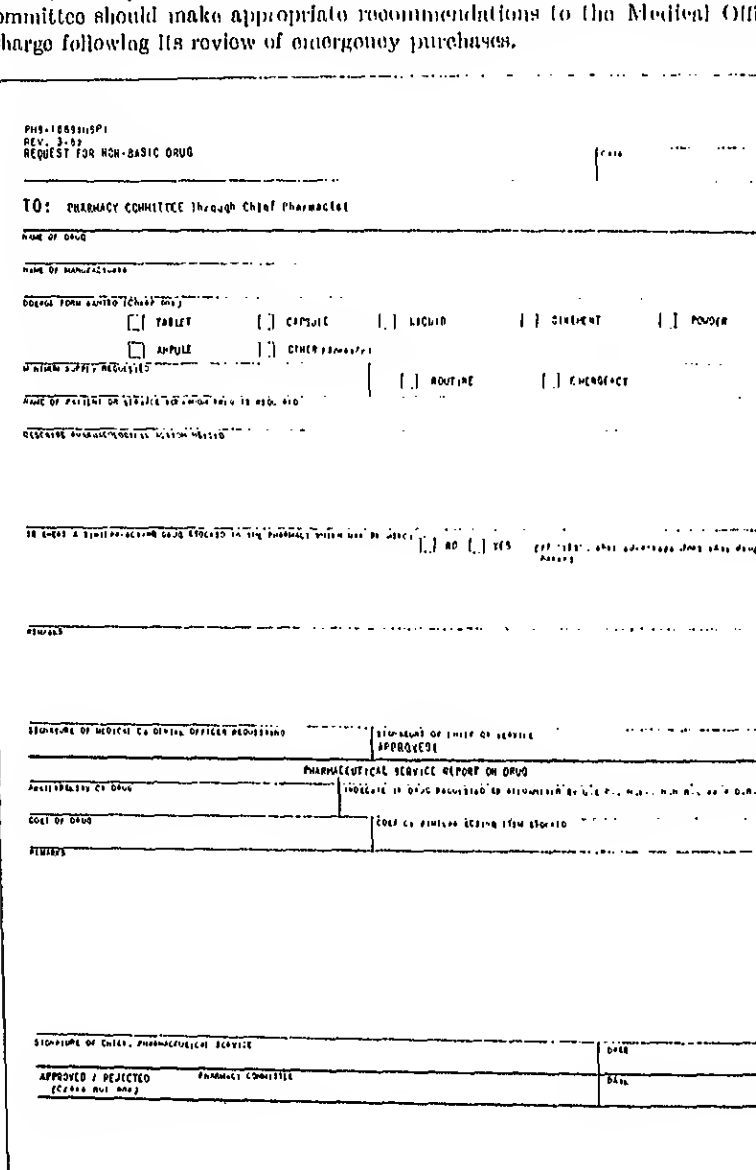
Basic Drugs—U. S. Public Health Service Hospitals and Clinics is furnished to all stations as a guide which may be expanded or otherwise altered to suit the wishes of the group concerned, as indicated in the Foreword of this manual.

Suggested rules governing admission of drugs to the station Basic Drug Manual:

(1) The committee will review requests for items not routinely stocked, upon the written request (Form 1689-HSP, available at the pharmacy) of a medical or dental officer, approved by his chief of service. Such request should contain a justification of the item requested, and a statement of the amount to be ordered, on the basis of specific patient or service needs.

(2) Requests should not ordinarily be made for items by trade names, when such items are also official in the U. S. Pharmacopeia or National Formulary. A

(4) *Emergencies.*—Emergency purchases of drugs not routinely stocke
quested on form PHS-1689 (HSP), reproduced below, and made under
established by the Medical Officer in Charge, should be reviewed at th
meeting of the pharmacy committee subsequent to such purchases. The pha
committee should make appropriate recommendations to the Medical Offi
Charge following its review of emergency purchases.



PHS-1689-1(SP)
REV. 3-69
REQUEST FOR NON-BASIC DRUG

DATE

TO: PHARMACY COMMITTEE through Chief Pharmacist

NAME OF DRUG

NAME OF MANUFACTURER

DOSAGE FORM WANTED (Check One)

[ ] TABLET [ ] CAPSULE [ ] LIQUID [ ] OINTMENT [ ] POWDER

[ ] AMPULE [ ] OTHER (Specify)

QUANTITY REQUESTED

[ ] ROUTINE [ ] EMERGENCY

NAME OF PATIENT OR SERVICE FOR WHOM DRUG IS NEEDED

REASON(S) FOR NON-STOCKED ITEM REQUEST

IS SUCH A SIMILAR-ACTING DRUG STOCKED IN THE PHARMACY WHICH MAY BE USED? [ ] NO [ ] YES (If "YES", what advantage does this drug have over the one stocked?)

REMARKS

SIGNATURE OF MEDICAL OR DENTAL OFFICER REQUESTING

SIGNATURE OF CHIEF OF SERVICE APPROVING

PHARMACEUTICAL SERVICE REPORT ON DRUG

AVAILABILITY OF DRUG

INCLUSION OF DRUG PROCESSED BY PHARMACIST IN U.S.P., N.F., N.N.R., or N.D.R.

COST OF DRUG

COST OF SIMILAR ACTING ITEM STOCKED

REMARKS

SIGNATURE OF CHIEF, PHARMACEUTICAL SERVICE

DATE

APPROVED / REJECTED (Circle One) PHARMACY COMMITTEE

DATE

BASIC DRUG LIST

ALLERGY, AGENTS USED IN.....

ANALGETICS.....

Salicylates

Acetylsalicylic Acid, U. S. P. (Aspirin)_____
Tablets, U. S. P., 0.3 Gm., 60 mg. (flavored)_____
Methyl Salicylate, U. S. P. (Wintergreen Oil)_____
Sodium Salicylate, U. S. P._____
Tablets, U. S. P., Enteric Coated, 0.3 Gm., 0.6 Gm.__

Opium Derivatives

Codeine Phosphate, U. S. P._____
Tablets, U. S. P., Hypodermic, 8 mg., 15 mg., 30 mg., 60 mg_____
Metopon Hydrochloride, N. N. R._____
Capsules, 3 mg_____
Morphine Sulfate_____
Injection, U. S. P., 10 mg. per cc., 15 mg. per cc_____
Tablets, U. S. P., Hypodermic, 8 mg., 10 mg., 15 mg___
Papaverine Hydrochloride, U. S. P._____
Injection, U. S. P., 60 mg. per 2 cc_____
Tablets, 0.1 Gm_____

Nonopiate, Addicting Analgetics

Meperidine Hydrochloride, U. S. P. (Demerol Hydrochloride)_
Injection, U. S. P., 100 mg. per 2 cc_____
Tablets, 50 mg_____

Others

Colchicine, U. S. P._____
Tablets, U. S. P., 0.6 mg_____
Neacinchophen, U. S. P._____
Tablets, U. S. P., 0.3 Gm_____
Acetophenetidin, U. S. P._____
Tablets, U. S. P., 0.3 Gm_____

(See also Agents Used in Dermatologic Practice)

Alcohols

Alcohol, U. S. P. (Ethyl Alcohol)

Isopropyl Alcohol, N. F.

Acetone

Acetone, N. F.

Antibiotics (see also Systemic Anti-infectives—Antibiotics).

Aureomycin Hydrochloride, U. S. P.

Ointment, 3%

Ointment, Ophthalmic, 0.1%

Powder to make 0.5% Solution, Ophthalmic

Bacitracin

Ointment, 500 units per Gm.

Ointment, Ophthalmic, 500 units per Gm.

Powder, 50,000 units vial

Chloroazodin

Chloroazodin, U. S. P. (Azochloramid)

Powder for Saline Solution

Solution, U. S. P. (1:500 in Triacetin)

Solution, Strong (1:125 in Triacetin)

Cresol

Saponated Cresol Solution, N. F.

Formaldehyde

Formaldehyde Solution, N. F.

Formaldehyde Instrument Solution

Hexachlorophene

Hexachlorophene

2% in suitable detergent; 3% in suitable detergent

Iodine

Iodine, U. S. P.

Iodine Tincture, U. S. P.

Silver

Silver Nitrate, U. S. P.

Surface Active Agents

Benzalkonium Chloride, U. S. P. (Zephiran)

Concentrated Solution, 12.8%

Trichomonacide

Iodochlorhydroxyquin, N. F. (Vioform)

Inserts (Suppositories)

Anthelmintics

Antimony Potassium Tartrate, U. S. P.

Ampuls, 1%, 5 cc.

Aspidium Oleoresin, U. S. P.

Capsules, 1 Gm.

Hexylresorcinol, U. S. P.

Pills, U. S. P., 0.1 Gm., 0.2 Gm.

Methylrosaniline Chloride, N. F. (Gentian Violet)

Tablets, Enteric Coated, 9 mg., 30 mg.

Solution, 1%

Quinacrine Hydrochloride, U. S. P. (Atabrine Dihydrochloride)

Tablets, 0.1 Gm.

Stibamine Glucoside, N. N. R. (Neostam Stibamine Glucoside)

Ampuls, Powder for Solution, 0.1 Gm., 0.5 Gm.

Tetrachloroethylene, U. S. P.

Capsules, U. S. P., 0.5 cc., 1.0 cc.

Antibacterial Drugs

Calcium Mandelate, U. S. P.

Tablets, U. S. P., 0.55 Gm. (Mandelic Acid, 0.5 Gm.)

Methenamine, U. S. P.

Tablets, U. S. P., 0.3 Gm., 0.5 Gm.

p-Aminosalicylic Acid, N. N. R.

Tablets, N. N. R., 0.5 Gm.

Sulfonamides

Sulfone Compounds:

Sulfoxone Sodium, N. N. R. (Diasone Sodium)

Tablets, N. N. R., 0.15 Gm.

Tablets, N. N. R., Enteric Coated, 0.33 Gm.

Antibiotics and Sulfonamides

Antibiotics

Auromycin Hydrochloride, U. S. P.

Capsules, U. S. P., 50 mg., 250 mg.

Ampul, 100 mg., Intravenous

Ointment, 3%: ½ oz.*, 1 oz.*

Ointment, Ophthalmic, 0.1%*

Powder, Ophthalmic (with Sodium Chloride, 62.5 mg. and Sodium Borate, 25 mg.)*

*See also Local Anti-Infectives.

Antibiotics and Sulfonamides—Continued

Antibiotics—Continued

Chloramphenicol, U. S. P. (Chloromycetin)
Capsules, 50 mg., 100 mg., 250 mg

Streptomycin Sulfate, U. S. P.
Ampuls, powder, 1 Gm., 5 Gm.

Dihydrostreptomycin Sulfate, U. S. P.
Ampuls, Powder, 1 Gm., 5 Gm.

Penicillin G Sodium (or Potassium), **U. S. P.**
Ampuls, 100,000 units to 5,000,000 units.

Penicillin Procaine, Aqueous Suspension
Disposable Injection Units, 300,000 units per cc.
Ampuls, 10 cc., 300,000 units per cc.

Penicillin Procaine in Oil Injection, U. S. P.
Disposable Injection Units, 300,000 units per cc.
Ampuls, 10 cc., 300,000 units per cc.

Penicillin Tablets, U. S. P., 100,000 units

Terramycin Hydrochloride, N. N. R.
Capsules, N. N. R., 250 mg.

Sulfonamides

Sulfadiazine, U. S. P.
Tablets, U. S. P., 0.5 Gm.

Meth-Dta-Mer-Sulfonamides, N. N. R.
Suspension, 0.5 Gm. per 4 cc.
Tablets, 0.5 Gm.

Succinylsulfathiazole, U. S. P.
Tablets, U. S. P., 0.5 Gm.

Sulfapyridine, N. F.
Tablets, N. F., 0.5 Gm.

Antiprotozoan Drugs

Antiamebic Drugs

Auromycin Hydrochloride, U. S. P.
Capsules, U. S. P., 50 mg., 250 mg.

Carbarsone, U. S. P.
Capsules, U. S. P., 0.25 Gm.
Tablets, U. S. P., 0.25 Gm.

Chloroquine Phosphate, U. S. P. (Aralen Diphosphate)
Tablets, 0.25 Gm.

Diiodohydroxyquinoline, U. S. P. (Diodoquin, Yodoxin)
Tablets, U. S. P., 0.65 Gm.

Emetine Hydrochloride, U. S. P.
Injection, U. S. P., 60 mg. per cc.
Tablets, Hypodermic, 30 mg., 60 mg.

Antimalarial Drugs

Chloroquine Phosphate, U. S. P.
(Aralen Diphosphate)
Tablets, 0.25 Gm.

Quinacrine Hydrochloride, U. S. P.
(Atabrine Dihydrochloride)
Tablets, 0.1 Gm.

Quinine Dihydrochloride, U. S. P.
Injection, N. F., 10 cc. containing 0.3 Gm.

Quinine Sulfate, U. S. P.
Capsules, U. S. P., 0.3 Gm.

Antisyphilitic Drugs

Penicillin (see Systemic Anti-Infectives—Antibiotics)

Antitrypanosomic Drugs

Suramin Sodium, U. S. P.
Ampuls, Powder, Sterile, 1 Gm.

Tryparsamide, U. S. P.
Ampuls, Powder, 1 Gm.

CARDIOVASCULAR DRUGS

Digitalis, U. S. P.
Tablets, U. S. P., 0.1 Gm.

Digoxin, U. S. P.
Injection, U. S. P., 1 cc., 0.5 mg.
Tablets, U. S. P., 0.25 mg.

Quinidine Sulfate, U. S. P.
Tablets, U. S. P., 0.2 Gm.

COUGH THERAPY, AGENTS USED IN

Ammonium Chloride, U. S. P.
Syrup, 0.2 Gm. in 4 cc. (Wild Cherry base)

Codeine Phosphate, U. S. P.
Tablets, U. S. P., 8 mg.
Syrup, 8 mg. per 4 cc. (Wild Cherry base)

Potassium Iodide, U. S. P.
Tablets, N. F., 0.3 Gm.
Syrup, 0.3 Gm. in 4 cc. (Glycyrrhiza base)

Absorbable Gelatin Sponge

Vitamin K

Tannic Acid, N. F.

Epinephrine Solution, U. S. P.

Respiratory Stimulants

Direct Stimulants

Reflex Stimulants

Sedatives and Hypnotics

Aldehyde Derivatives

Barbituric Acid Derivatives

Spasmolytics

Amyl Nitrite, U. S. P.

Atropine Sulfate, U. S. P.

Scopolamine Hydrobromide, U. S. P.

Sympathomimetic Amines

Epinephrine, U. S. P.

Phenylephrine Hydrochloride, U. S. P.

Nordefrin Hydrochloride, A. D. R., (Cobefrin)

Vitamins

Miscellaneous Drugs

Operative

Sodium Fluoride

Sodium Fluoride Paste

Zinc Oxide, U. S. P.

Eugenol, U. S. P.

Periodontia

Zinc Chloride, N. F.

Trichloroacetic Acid, U. S. P.

Compound Benzoin Tincture, U. S. P.

Endodontia

Hydrogen Peroxide, 30%

Mouth Wash

Sodium Bicarbonate and Sodium Chloride

Pharmacologic Effects

Anti-Infective Agents—Antibacterial

Antibiotics

Auroomycin, U. S. P.

Bacitracin, N. N. R.

Tyrothricin Solution, U. S. P.

Mercurials

Ammoniated Mercury, U. S. P. (1–10%)

Mercury Bichloride, U. S. P. (1:1000)

Others

Hydrogen Peroxide Solution, U. S. P.

Iodochlorhydroxyquin, U. S. P. (Vioform)

Methylrosaniline Chloride, N. F.

Antifungus Agents

Benzoic Acid, U. S. P.

Iodine, U. S. P.

Methylrosaniline Chloride, N. F.

Potassium Permanganate, U. S. P.

Salicylic Acid, U. S. P. 74, 75, 76, 7

Sodium Thiosulfate, N. F.

Undecylenic Acid, N. F., and Salts 7

Copper Undecylenate

Zinc Undecylenate, N. F.

Antiparasitic Agents

Benzene Hexachloride, U. S. P.

Precipitated Sulfur, U. S. P. 7

Antiphlogistics

Aluminum Acetate Solution, U. S. P.

Boric Acid, U. S. P. (1–2% Solution)

Ointment ("Aveeno")

Potassium Permanganate, U. S. P., 1:1000-1:10000, fresh solutions

Sodium Chloride Solution, Isotonic, U. S. P.

Starch, U. S. P.

Antipruritic and Analgetic Agents—Local

Camphor, U. S. P., ⅛–5%

Chlorol Hydrate, U. S. P., 1–5%

Menthol, U. S. P., ⅛–½%

Phenol, U. S. P., ½–1%

Sodium Thiosulfate

Antipruritic and Analgetic Agents—Oral

Histamine-Antagonizing Agents

Diphenylpyraline, U. S. P. (Prantone)

Agents Used, Topical

Solutions

Baths—Colloid

Starch and Sodium Bicarbonate

Oatmeal

Baths—Medicated

Potassium Permanganate (1:16000-1:32000)

Sulfur Bath: Sulfurated Lime Solution, N. F.

Tar Bath: Coal Tar Solution, N. F.

Wet dressings

Aluminum Acetate Solution, U. S. P.

Aluminum Acetate Solution Powder

Potassium Permanganate Tablets, N. F., 0.3 Gm.

Sodium Chloride

Solutions for specific use

Acetic Acid (1/2-1%)

Aluminum Chloride Solution

Chloroformic Anthralin Solution

Petroleum Benzin, U. S. P.

Boric Acid Solution

Coal Tar Solution, N. F.

Chloroformic Coal Tar Solution, N. F.

Flexible Collodion, U. S. P.

Copper and Zinc Sulfates Solution

Copper Undecylenate Solution

Hydrogen Peroxide Solution, U. S. P.

Iodine Tincture, U. S. P.

Methylrosaniline Chloride Solution, 2%

Podophyllum Resin, Alcoholic

Podophyllum Resin, Oily

Salicylic Collodion, N. F.

Silver Nitrate Solution

Sodium Thiosulfate Solution

Sulfurated Lime Solution, N. F.

Tar Collodion

Tyrothricin Solution, U. S. P.

Powders

Sodium Bicarbonate and Talc Powder

Talc

Compound Undecylenic Acid Powder

Lotions and Liniments

Calamine Lotion

Scalp Lotions:

Chloral Hydrate

Chloral Hydrate, Oily

Resorcinol

Resorcinol, Oily

Tar

Lotions and Liniments—Continued

Sunlight Protective:

Cycloform Lotion

White Lotion

Zinc Oxide Lotion

Zinc Oxide Oil Lotion

Calamine *Liniment*

Ointments and Pastes

Ointments

Anthralin, various strengths

Aureomycin, 3%

Bacitracin

Benzene Hexachloride

Betanaphthol-Sulfur

Benzoic and Salicylic Acid

Coal Tar

Hydrophylic

Ichthammol-Zinc Oxide

Iodochlorhydroxyquin Cream

Juniper Tar Ointment

Mercury, Ammoniated

Petrolatum, White

Pine Tar

Rose Water

Sulfur

Undecylenic Acid, Compound

Zinc Oxide

Pastes

Aluminum Acetate

Zinc Gelatin

Zinc Oxide

Plasters

Salicylic Acid

Soap Substitutes

Tar and Tar Derivatives

Ichthammol

Coal Tar

Coal Tar Solution

Chloroformic Coal Tar Solution

Wood Tars (Juniper; Pine)

Cascara Sagrada, U. S. P.

Cascara Sagrada Extract Tablets, U. S. P., 0.3 Gm.

Aromatic Cascara Sagrada Fluidextract, U. S. P.

Castor Oil, U. S. P.

Cathartics, Mechanical and Lubricant (Emollient)

Liquid Petrolatum, U. S. P.

Emulsion, U. S. P.

Methylcellulose, N. F.

Solution, 1%

Choleretics

Ox Bile Extract, U. S. P.

Tablets, U. S. P., Enteric Coated, 0.3 Gm.

Dehydrocholic Acid, N. F.

Tablets, N. F., 0.25 Gm.

HEMATICS

Antianemia Drugs

Ferrous Sulfate, U. S. P.

Tablets, U. S. P., Enteric Coated, 0.3 Gm.

Exsiccated Ferrous Sulfate Tablets, U. S. P., Enteric Coated, 0.2 Gm.

Liver Injection, U. S. P.

Ampuls, U. S. P., 10 cc., 15 units per cc.

Powdered Stomach, U. S. P.

Folic Acid, U. S. P.

Tablets, U. S. P., 5 mg.

Vitamin B_{12}, U. S. P.

Injection, U. S. P., 15 *mcg.* per cc. and 30 *mcg.* per cc.; various sizes.

Coagulants

Absorbable Gelatin Sponge, U. S. P. (Gelfoam)

Epinephrine, U. S. P.

Phenylephrine Hydrochloride, U. S. P.

Thrombin, U. S. P.

Vitamin K (see Vitamins)

Anticoagulants

Bishydroxycoumarin, U. S. P. (Dicumarol)

Tablets, 25 mg., 50 mg., 0.1 Gm.

Heparin Sodium, U. S. P. (Heparin)

Injection, U. S. P., Ampuls, 1,000 units per cc., 10 cc.; 5,000 units per cc., 1 cc. and 10 cc.; 10,000 units per cc., 4 cc.

Heparin Sodium, Repository Form, N. N. R.

Ampuls, 20,000 units, 1 cc.

Repository Heparin Sodium with Vasoconstrictors, Ampuls,

Carbochol, U. S. P. (Doryl)

Methacholine Chloride, U. S. P. (Mecholyl chloride)

Ampuls, Powder, 25 mg

Cholinesterase Inhibitors

Physostigmine Salicylate, U. S. P.

Powder

Tablets, Hypodermic, 1 mg., 1.2 mg., 1.5 mg

Neostigmine Bromide, U. S. P. (Prostigmine Bromide)

Prostigmine Bromide Tablets, 15 mg

Neostigmine Methylsulfate, U. S. P. (Prostigmine Methylsulfate)

Ampuls, Prostigmine Methylsulfate, 1:4000, 1 cc.; 1:2000, 1 cc

Direct Receptor Effect

Pilocarpine Hydrochloride, U. S. P.

Ointment, Ophthalmic, 1%

Powder

Tablets, Hypodermic, 5 mg

PARENTERAL FLUIDS

Dextrose Injection, U. S. P., 5% (in distilled water)

Dextrose Injection, 5%, in Isotonic Sodium Chloride Solution

Dextrose Injection, 5% with 5% Protein Hydrolysate

Dextrose Injection, U. S. P., 10% (in distilled water)

Sodium Chloride Solution, Isotonic, U. S. P.

Whole Blood

Normal Human Serum Albumin, U. S. P.

Potassium Chloride Solution, 40 milliequivalents (20 cc., 2.98 Gm.)

Sodium Bicarbonate Solution, 5%

Sodium Chloride Solution, 5%

Sodium Lactate Injection, U. S. P., 1/6 molar

SCLEROSING AGENTS

Sodium Morrhuate, U. S. P.

Injection, U. S. P., *Ampuls*, 5%, 2 cc., 5 cc., 25 cc.

Dextrose, U. S. P.

Injection, U. S. P., 50%, 50 cc.

Barbituric Acid Derivatives

Long Action

Phonobarbital, U. S. P.

Tablets, U. S. P., 15 mg., 30 mg., 0.1 Gm.

Elixir, U. S. P., 15 mg. per 4 cc.

Phenobarbital Sodium Injection, U. S. P., 0.12 Gm., solution in Propylene Glycol or similar suitable solvent.

Phenobarbital Sodium Tablets, U. S. P., Hypodermic, 60 mg.

Phenobarbital Sodium, Sterile, U. S. P., 0.12 Gm. Powder (for aqueous solution immediately prior to injection).

Intermediate Action

Pentobarbital Sodium, U. S. P.

Capsules, U. S. P., 50 mg., 0.1 Gm.

Suppositories, 0.12 Gm.

Injection, U. S. P., Powder, 0.25 Gm.

Short Action

Secobarbital Sodium, N. N. R. (Seconal Sodium)

Capsules, 50 mg., 0.1 Gm.

Suppositories, 0.12 Gm., 0.2 Gm.

Ampuls, 0.25 Gm.

Ultra-Short Action

Thiopental Sodium, U. S. P. (Pentothal Sodium) (see General Anesthetics)

Ampuls, 0.5 Gm., 1 Gm., 5 Gm. (multiple dose ampul).

Hydantoin Derivatives

Diphenylhydantoin Sodium, U. S. P. (Dilantin Sodium)

Capsules, 30 mg., 0.1 Gm.

Trimethadione, U. S. P. (Tridione)

Capsules, 0.3 Gm.

Tablets (candied), 0.15 Gm.

Solution, 0.15 Gm. per 4 cc.

Alcoholic Preparations

Whisky, N. F.

Aldehyde Derivatives

Paraldehyde, U. S. P.

Atropine and Related Compounds

Atropine Sulfate, U. S. P.

Tablets, U. S. P., 0.06 mg., 0.25 mg., 0.3 mg., 0.4 mg., 0.6 mg.

Belladonna Tincture

Homatropine Hydrobromide, U. S. P.

Scopolamine Hydrobromide, U. S. P. (Hyoscine Hydrobromide)

Tablets, U. S. P., 0.3 mg., 0.4 mg., 0.6 mg.

Homatropine Methylbromide, U. S. P.

Tablets, 2.5 mg., 4 mg.

Barbituric Acid Derivatives—see Sedatives and Hypnotics.

Narcotics

Meperidine Hydrochloride, U. S. P. (Demerol Hydrochloride), see Analgetics.

Papaverine Hydrochloride, U. S. P.

Tablets, U. S. P., 0.1 Gm.

Injection, U. S. P., *Ampuls*, 60 mg. per 2 cc.

Nitrites

Amyl Nitrite, U. S. P.

Ampuls for inhalation, 0.2 cc.

Glyceryl Trinitrate, U. S. P. (Nitroglycerin)

Tablets, 0.4 mg., 0.6 mg.

Mannitol Hexanitrate, U. S. P.

Tablets, 15 mg., 30 mg.

Sympathomimetic Drugs (see Epinephrine and Ephedrine, under Sympathomimetic Amines)

Xanthine Derivatives

Aminophylline, U. S. P.

Tablets, U. S. P., Enteric Coated, 0.1 Gm., 0.2 Gm.

Injection, U. S. P., *Ampuls*, Intramusc., 0.5 Gm. in 2 cc., Intrav., 0.25 Gm. in 10 cc.

Suppositories, U. S. P., 0.5 Gm.

Theobromine Calcium Salicylate, U. S. P.

Tablets, U. S. P., Enteric Coated, 0.5 Gm.

B Complex Vitamins—Continued

Triasyn B Tablets, U. S. P. (2 mg. Thiamine Hydrochloride, 3 mg. Riboflavin, 20 mg. Nicotinamide)----------

Vitamin B Complex Injection—various sizes----------

Vitamin B Complex Liquid----------

Vitamin B_{12}—see Hematics.

Folic Acid—see Hematics.

Vitamin K

Menadione Sodium Bisulfite, U. S. P----------

Injection, U. S. P----------

Ampuls, 3.84 mg. (2 mg. menadione), 1 cc----------

Ampuls, 72 mg. menadione, and 27.5 mg. sodium bisulfite in 10 cc----------

Tablets, 5 mg----------

Vitamin K_1----------

Ampuls, 1 Gm., 5 Gm----------

Multiple Vitamin Therapy

Hexavitamin Tablets, U. S. P., (Vitamin A, 5,000 units; Vitamin D, 400 units; Ascorbic Acid, 75 mg.; Thiamine Hydrochloride,2 mg.; Riboflavin, 3 mg.; Nicotinamide, 20 mg.)--

Chapter 1.

AGENTS USED IN ALLERGY

Allergenic extracts are employed for the diagnosis and control of allergic diseases. They are particularly useful in identifying specific excitants of the conditions under examination, indicating (following diagnosis) either desensitization, or, frequently, avoidance of the specific cause.

Several forms of the diagnostic test have been employed. The two forms in common usage are the scratch test and the intracutaneous test. The intracutaneous test is favored by many clinicians. The technique of the intracutaneous test consists of injecting from 0.01 to 0.02 cc. of the stock test extract between the skin layers of the arm, shoulders, or back. The test areas ordinarily may be read within 10 minutes, sometimes earlier if positive. A markedly positive reaction consists of a pale, tense swelling typically showing irregularity of the periphery, "pseudopods", and usually surrounded with a zone of erythema. A doubtful reaction is one in which pseudopods do not appear.

In cases in which a procedure of desensitization may be properly applied it will be found that a marked positive reaction with pseudopod formation can be elicited by the intracutaneous test with the appropriate extract. Since the stock test extract causes a markedly positive reaction, this would be too strong to initiate desensitization. The extract should be further diluted 1 to 1,000, 1 to 10,000, 1 to 100,000, and sometimes 1 to 1,000,000. The correct dilution used to initiate treatment is a matter of clinical judgment; but in general should be a dilution which just fails to give a positive skin test. The subsequent doses of the diluted material are given at weekly or semiweekly intervals. As treatment proceeds, stronger dilutions are used and a smaller percentage increase in dosage may be advisable. Also, the interval between injections is lengthened. The final dosage and maintenance dosage are matters of judgment by the physician. The aim in treatment is to find a dose which approaches the limit of tolerance of the patient. Frequently it may be necessary to continue monthly or more frequent injections. In cases of multiple sensitivity, the injections of several extracts are customarily made simultaneously.

Various extracts are available for allergenic testing. These include a variety of pollens, molds, foods, and others.

See also "Histamine-Antagonizing Agents," p. 98; and "Desensitization Procedures" (Serums and Vaccines), p. 122.

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Chapter 2.

ANALGETICS

Analgetic drugs depress pain receptive mechanisms centrally or p and reactions to pain, without producing loss of consciousness. Som may serve maluly to reduce the reactions to pain. In the case of ana as morphine and other opium derivatives, their hypnotic action aids t effect. The analgetics considered in this section are the salicylat meperidine (demerol), colchicine, neocinchophen, and acetophenetidi pyrine has not been included because of agranulocytosis which has re its use.

SALICYLATES

Salts and esters of *salicylic acid* are used instead of the acid to obtain action and avoid its irritating effect on mucosa. These compound to produce salicylic acid and are classified as (1) simple salicylate s salicylate); and (2) esters of salicylic acid (acetylsalicylic acid, methy Although the salicylic acid equivalent of sodium salicylate and of ac acid are within 10 percent of each other, the effectiveness of acetylsal about 1½ times that of an equal amount of sodium salicylate.

The *salicylates* are particularly effective against the pain of acut fever. They are also effective in relieving headache, myalgia, arthr salicylate ion also exerts antipyretic effect, through the hypothal accompanying increased sweating. There is no effect on normal t Children tolerate salicylates well and larger doses may be used than iated by dosage rules.

Toxicity. While acetylsalicylic acid is less irritating to the stom sodium salicylate, mucosal irritation may still occur particularly wi frequent doses are taken. Irritant action may lead to gastric ulcerati must always be considered. "Salicylism" may occur. Though 10 of sodium salicylate have caused death in some adults, larger doses taken by others without serious effect.

Treatment of salicylate poisoning. Gastric lavage with 5% so bonate solution. Follow by 15 Gm. of sodium sulfate to hasten ex the intestinal tract. Correct salt and fluid loss as indicated.

ACETYLSALICYLIC ACID, U. S. P. White, crystalline powder, in the presence of moisture to form acetic and salicylic acids. It is aqueous suspensions and should be prescribed in solid dry form.

U. S. P. usual dose: 0.3 Gm. (5 gr.).

Acute rheumatic fever. 0.6 to 1 Gm. every hour until symptom obtained or until mild salicylism appears. A total of 6 to 10 grams required. Wait 12 hours and resume with maintenance dose of 0.6 4 hours* during the day until all signs of active infection have been week or 10 days.

*Pharmacologically and perhaps clinically, 0.3 Gm. every 2 hours would provide for effect with the same total dose.

Dosage forms: Acetylsalicylic Acid Tablets, U. S. P. 60 mg. (1 gr.); 0.3 Gm. (5 gr.) Enteric coated tablets may be used if necessary to avoid gastric irritation.

METHYL SALICYLATE, U. S. P. (Wintergreen Oil.) Colorless or yellowish liquid having the odor of wintergreen. It is obtained synthetically, or by distillation, from gaultheria leaves or from betula bark. Except for its use as a flavor, methyl salicylate is reserved for external use. It is a good rubefacient. Taken internally, it is highly toxic, 30 cc. usually being fatal.

SODIUM SALICYLATE, U. S. P. White crystalline powder; very soluble in water (1 in 0.9) and freely soluble in alcohol (1 in 9.2).

U. S. P. usual dose. 1 Gm. (15 gr.). May be repeated every 3 or 4 hours. It is irritant to the stomach mucosa by reason of precipitation of salicylic acid by the hydrochloric acid of the stomach. This effect may be avoided by the use of enteric coated tablets.

Acute rheumatic fever. 1 to 1.3 Gms. every hour until effect obtained or until mild salicylism appears. A total of 8 to 13 grams is usually required. Wait 12 hours and resume with maintenance dose of 1 Gm. every 4 hours during the day until all signs of active infection have been absent for a week or 10 days.

Administration of sodium salicylate by vein. Such use for analgetic effect is dangerous and is unjustified.

Dosage forms. Sodium Salicylate Tablets, U. S. P., 0.3 Gm. (5 gr.); 0.6 Gm. (10 gr.) (enteric coated). A liberal amount of water should be taken if uncoated tablets are used. If necessary to give in solution, Compound Sarsaparilla Syrup, U. S. P., or Glycyrrhiza Syrup, U. S. P., are good masking vehicles.

OPIUM DERIVATIVES

This group of drugs is derived from opium, an exudate obtained from the poppy capsule. The U. S. P. opium must yield not less than 9.5% anhydrous morphine. In addition to morphine, more than 20 other naturally occurring alkaloids have been identified. The only important ones are codeine and papaverine. Chief pharmacologic effects of opium arise from the morphine present, the content of other alkaloids being too low to cause any significant modification of the morphine action. Therefore, the use of opium rather than morphine probably has no therapeutic advantage.

Morphine and codeine chemically are phenanthrene derivatives, and papaverine is a benzylisoquinoline derivative. There is a marked pharmacologic difference between these two chemical groups. The phenanthrene alkaloids act mainly on the central nervous system, and also contract smooth muscle. The benzylisoquinoline alkaloids have very little effect on the central nervous system but in adequate doses have a significant antispasmodic effect on smooth muscle.

CODEINE PHOSPHATE, U. S. P. Codeine, which is present only in small amounts in opium, is prepared by methylating morphine. As an analgetic, codeine is much less effective than morphine. In contrast to morphine, it does not produce proportionately greater narcotic effect with increasing doses. If 30 mg. (½ gr.) of codeine are not effective, larger doses usually have no additional analgetic effect and will cause undue side effect. Codeine has considerably less respiratory depressant action than morphine, and there is less tendency to nausea

Codeine phosphate is preferable to the sulfate because of its great
(1:2.5 for the phosphate, and 1:30 for the sulfate).

Dosage. 30 mg. (½ gr.). *Cough:* 8 mg. (⅛ gr.) to 10 mg. (⅙ gr.
Analgesia: 15 mg. (¼ gr.) to 30 mg. (½ gr.) orally or subcut.

Although it is customary to prescribe codeine in quantities of
usually is in excess of the effective dose of 8 mg. to 10 mg.

Dosage forms. Tablets. U. S. P., 8 mg. (⅛ gr.), 15 mg. (¼
(½ gr.), 60 mg. (1 gr.).

METOPON HYDROCHLORIDE, N. N. R. (7-methyldihydro
hydrochloride). Its limited analgetic power and the ease with whi
develops makes morphine inadequate for the clinical management of s
with severe and chronic pain. The need for a drug with more ana
than morphine in the relief of severe chronic pain and less danger of t
addiction can best be met with metopon hydrochloride. Other stron
tions, such as dihydromorphinone (Dilaudid), desomorphine, he
much greater liability to tolerance and addiction.

Because of its restricted usefulness and since it seems to potentia
atory depressant effects of other drugs (e. g., anesthetics, sedatives
able only in capsules (3 mg.) for oral administration. This is no ha
field of usefulness.

Dosage. 6 to 9 mg. orally at intervals of 4 to 6 hours for the cont
pain.

Dosage forms. Capsule, 3 mg.

MORPHINE SULFATE, U. S. P. The predominant action is o
nervous system and on the intestine. Doses up to 15 mg. have
effect, not necessarily followed by sleep; larger doses (15 to 20 mg.)
on sleep. Morphine *depresses respiration,* the degree of depression be
proportion to the size of the dose. It is more depressant to resp
codeine. In small doses, the *cough reflex is dulled;* in large doses, it
However, its addictive properties and constipating effect make it l
than codeine for cough therapy. Morphine causes *contraction of sm*
except those activating blood vessels. This action is utilized in
diarrhea. Morphine, as well as other opium alkaloids and opium it
local effect in the relief of pain. Their use, for local effect, in sup
ointments therefore is irrational.

Acute poisoning. Toxic dose for adults is about 60 mg. (1
than average doses are tolerated when severe pain is present. Infan
myxedematous individuals, and patients having liver disease are
susceptible to morphine. Doses of 250 mg. (approximately 4 gr.)
death. *Treatment.*—If taken by mouth, gastric lavage with 1:2,00
permanganate solution (if not available, 2 cc. Iodine Tr. per 500
gastric lavage, introduce 15 Gm. sodium sulfate, well diluted, into
to hasten elimination through the bowel. Avoid emetics as they
ineffective and tend to increase depression. Keep patient awake
If in deep coma, use artificial respiration; continuous oxygen thera
24 hours. For stimulation of respiration, give 0.5 Gm. caffeine and
soate subcut. or intramusc.; or ounces of strong black coffee. Ephe
20 to 40 mg. intramusc.; or amphetamine sulfate, 10 to 40 mg. (1 to
sol.) intramusc. followed by 10–20 mg. (1 to 2 cc.) every half hour

spasm, especially in renal or biliary colic. The intravenous route is often useful in severe coronary pain.

Spasmogenic action in diarrhea. 5 mg. (1/12 gr.) to 10 mg. (1/6 gr.). Smaller doses may be given as desired, without resorting to unnecessarily complex preparations, such as Camphorated Opium Tincture (morphine content, 1.8 mg. (approx. 1/30 gr.) per 4 cc.). Aside from tradition, the use of the camphorated tincture probably is related to its status as a Federal "exempt" narcotic preparation, and the attendant ease in obtaining it.

Preanesthetic use. 10 to 15 mg. subcut. 1 to 1½ hours before induction of anesthesia, or given in equally divided doses 2 hours and 1 hour respectively, before anesthesia. Its constipating effect must be considered in connection with operations in the gastrointestinal tract, as well as its respiratory depressant effect. Due to morphine miosis, it becomes difficult to evaluate the pupil size as a sign of anesthesia.

Dosage forms

Tablets, U. S. P., 8 mg. (1/8 gr.), 10 mg. (1/6 gr.), 15 mg. (1/4 gr.).

Injection, U. S. P., 1 cc. containing 10 mg. (1/6 gr.); 1 cc. containing 15 mg. (1/4 gr.).

PAPAVERINE HYDROCHLORIDE, U. S. P. See under "Spasmolytics," page 133.

NONOPIATE, ADDICTING ANALGETICS

MEPERIDINE HYDROCHLORIDE, U. S. P. (Demerol Hydrochloride). This synthetic drug was developed as a possible atropine substitute. While it does possess some atropine-like action, its chief therapeutic value lies in its combined analgetic and spasmolytic effects. In this it is unique since the opiates increase the tone of smooth muscle. As an analgetic, meperidine is intermediate between morphine and codeine. However, it is not altogether reliable from patient to patient, or in the same patient from time to time.

It is probably as good as any other spasmolytic for the gastrointestinal and genitourinary tracts. It is an inferior sedative. It possesses a nitritoid action which makes its use on ambulatory patients undesirable. It possesses very definite addiction liability. Like the opiates, it is contraindicated for use in patients with head injury because it dilates blood vessels and increases blood flow. Cortical hyperirritability has been observed as a result of its abuse. Used in obstetrics, it may not be as depressant to fetal respiration as the opiates.

Dosage. 50 to 150 mg. every 3 to 4 hours; 100 mg. is the usual dose. It may be given by any route. Its action begins in 20 minutes and lasts about 3 hours. Intravenous use is usually avoided because of the nitritoid effect and the increased danger of addiction. Parenteral administration has little advantage over oral administration.

Dosage form. Demerol Hydrochloride *tablets*, 50 mg.; *ampuls*, 2 cc. containing 100 mg.

saffron). It is yellowish in color, [illegible]
poisonous and *its sole therapeutic use is for the relief of acute gout.*
entirely empirical, and the drug has practically no value in chronic go
is relief of pain, swelling, and redness in acute gout; its mode of ac
clear. Diarrhea usually occurs as a side effect, poisoning being ov
increased gastrointestinal symptoms such as severe pain, nausea,
The kidneys may be affected, resulting in hematuria and oliguria

Treatment of poisoning. Lavage; antishock therapy; morphine an
to relieve abdominal distress.

U. S. P. usual dose. 0.5 mg. (1/120 gr.) *Acute gout:* 1 mg. every 2
for 4 or 5 doses. Do not continue drug after pain is relieved. St
severe nausea, gastric distress, weakness, hematuria, or oliguria occur.

Dosage forms. Tablets, U. S. P., 0.5 mg. (1/120 gr.).

NEOCINCHOPHEN

NEOCINCHOPHEN, U. S. P. is the ethyl ester of 6-methyl-2-phen
4-carboxylic acid. This derivative of cinchophen was introduced as les
than the parent drug; there is still question as to the relative toxici
compounds, and it must be recognized that both are potentially toxic

Neocinchophen has been favored by some primarily for the treatme
Its potentially harmful effect on the liver renders it undesirable for
as an analgetic.

Toxic manifestations. Acute hepatitis, evidenced by appearance o
albuminuria, diarrhea, vomiting.

U. S. P. usual dose. 0.3 gm (5 gr.) *Acute or chronic gout:* 0.5
Gm. 3 times daily, taken with large quantities of water. Sodium
usually is given concurrently to diminish gastric distress and to preve
tation of urates.

Dosage form. Tablets, U. S. P., 0.3 Gm. (5 gr.).

ACETOPHENETIDIN

ACETOPHENETIDIN, U. S. P. is a coal tar derivative originally
under the trade name, "phenacetin." It is a white powder slightly
water (1:1,300).

Acetophenetidin acts as an antipyretic analgetic, its mode of a
similar to that of the salicylates. It is not effective, as are the sal
gout or rheumatic fever, and it is much more toxic than the salicylates
Acetophenetidin should not be used over a period of days or for any
use. If average doses are not effective, larger doses usually will not
either.

U. S. P. usual dose. 0.3 Gm. (5 gr.); may be repeated every 3

Dosage forms. Tablets, U. S. P., 0.3 Gm. (5 gr.).

General anesthetics act to produce unconsciousness and muscular relaxation by depression of the central nervous system. They act first on the higher cortical centers (analgetic stage); second, on the higher motor centers (excitement stage); third, on the spinal cord (surgical stage); fourth, on the medulla (paralytic, or fatal stage). Changes in respiration, skin color, pupillary and laryngeal movement, and pulse indicate progress through the various stages.

General anesthetics are of three general types: *volatile liquids* (ether, ethyl chloride, trichloroethylene); *gases* (nitrous oxide, ethylene, cyclopropane); *solids* (thiopental sodium).

VOLATILE LIQUIDS

ETHER, U. S. P. Volatile liquid; miscible with water (1 in 15) and with alcohol (all proportions). It is highly inflammable and explosive and should not be used near an open flame or electric or static spark. Cautery must not be used about the head or neck of the patient, and only with special care about other parts of the body.

A maintenance concentration of 4 to 6 volumes percent in inhaled air usually is sufficient for surgical anesthesia. The fatal concentration ranges between 8 and 11 volumes percent. Approximately 150 cc. by the "cone" method, and 250 cc. by the drop method may maintain anesthesia for about 1 hour. Ether is one of the safest of general anesthetics. Small amounts added to gaseous anesthetics aid in muscular relaxation.

Contraindications.—Acute respiratory infection, chronic pulmonary disease (tuberculosis, bronchiectasis, etc.), advanced renal disease. As with other anesthetics, ether must be used with caution in advanced heart disease.

ETHYL CHLORIDE, U. S. P. See "Local Anesthetics," p. 41.

TRICHLOROETHYLENE, U. S. P. Contains not less than 99% and not more than 99.5% of C_2HCl_3. The remainder consists of alcohol. Clear, colorless, volatile liquid having characteristic odor resembling that of chloroform. It is slowly decomposed by light in the presence of moisture and is not inflammable. It is practically insoluble in water but miscible with ether, alcohol, and chloroform, and dissolves most fixed and volatile oils.

Action and uses. Trichloroethylene is a general anesthetic whose use has been limited chiefly to the treatment of trigeminal neuralgia (tic douloureux). This is not a selective action as sometimes assumed but probably is a result of the central depressant effect of the drug and mild anesthesia on branches of the fifth cranial nerve.

Dosage. 1 cc., by inhalation, three to four times daily. The drug should be inhaled in a reclining position.

Dosage form. Ampuls for inhalation; 30 cc. bottles.

GASES

CYCLOPROPANE, U. S. P. (trimethylene). Colorless gas of characteristic odor and pungent taste, heavier than air, inflammable and explosive; freely soluble in water (1 in 2.7) and alcohol.

margin of safety between anesthetic and toxic concentrations for use as general anesthetic. Induction and recovery with cyclopropane are slower than with ethylene but more rapid than with ether.

Administration. By inhalation in a closed circuit type apparatus in 15% to 30% concentration with at least 20% oxygen. Preanesthetic medication is desirable.

Caution.

a. Cyclopropane *does not stimulate respiration* as do many other anesthetic agents and *for this reason preoperative sedation with respiratory depressants must be used with caution.*

b. The signs of Guedel for other anesthetic agents differ from those for cyclopropane, so that familiarity with the signs of the stages of anesthesia for cyclopropane is absolutely necessary in the administration of the agent. Respiration, skin color, larynx, and pupillary signs cannot be used. Changes in pulse are best danger signals—arrhythmias, slowing of heart beats to 50 or less per minute, or definite tachycardia. The second stratum of the surgical stage of anesthesia is reached in about 5 minutes; unconsciousness in from 20 seconds to 3 minutes.

c. Open flames, sparks, electric cauteries may cause explosions.

d. Transient cardiac arrhythmias, particularly ventricular tachycardia, may develop and epinephrine should not be employed.

ETHYLENE, U. S. P. (CH_2:CH_2) is a gas which acts as an aliphatic narcotic. It has comparatively low activity, but due to its high volatility, acts as a very rapid anesthetic. Recovery also is prompt (2 minutes). Ethylene is used with oxygen in ratio of about 80% to 20% respectively. Vital functions are affected only slightly. Induction is easier and faster than with ether; it is safer than ether; the after-effects of ethylene anesthesia are minimal. In comparison with nitrous oxide, ethylene does not cause asphyxia, the anesthesia is deeper and recovery more prompt. The only disadvantage is its extreme explosiveness.

NITROUS OXIDE, U. S. P. Colorless gas, without appreciable odor or taste. It is supplied compressed into a liquid, becoming gaseous upon release of pressure.

Actions and uses. Nitrous oxide is one of the safest anesthetics, especially for short operations. It acts rapidly, by direct narcosis. Inhalation of the undiluted gas causes exclusion of oxygen and a resulting asphyxial effect. This method usually is used in dentistry, the gas being removed when the asphyxial stage is reached, leaving enough anesthesia for the completion of a short operation. Special methods of mixing oxygen with the nitrous oxide permit longer anesthesia. Nitrous oxide is also used for induction in ether anesthesia.

Recovery from nitrous oxide anesthesia is prompt and lacking in after effect. It should not be used in undiluted form. Not safe in patients having cardiac lesions; in elderly patients with advanced arteriosclerosis; in brain operations; and in obese or anemic patients.

SOLIDS

THIOPENTAL SODIUM, U. S. P. (Pentothal Sodium) (ethyl 1-methyl butyl thiobarbiturate). A stable powder except in the presence of moisture. Dissolves readily in water forming a yellow alkaline solution.

Action and uses. Used intravenously as a general anesthetic for selected surgical operations of brief duration. Very useful to prevent pain from removal of

to be of prognostic assistance in determining the benefit to be expected from neurosurgical treatment of patients with hypertension and Raynaud's disease.

Administration. Thiopental sodium as an intravenous general anesthetic should be administered only by competent anesthetists with special experience in its use. Once the drug has been injected the depth of anesthesia can no longer be controlled by the anesthetist. There is no accurate method of determining the correct amount to be given (such as age and weight) since individuals may vary greatly in their responses. The proper dose for one patient may be too toxic for another. Slow injection and fractional dosage, in accordance with the physical signs of the patient during the course of the administration, are essential to the proper use of thiopental sodium.

The drug usually is injected into the median basilic or cephalic vein in the antecubital fossa. An injection of 4 to 6 cc. of a freshly prepared 2.5 percent solution (0.1 to 0.15 Gm.) is made in 10 to 15 seconds. Injection is stopped for 30 to 35 seconds to permit the full effect to be observed (patient usually is asleep). Injection is then continued at the rate of 4 to 8 cc. in 1 to 3 minutes to a total of 14 to 25 cc. (0.35 to 0.625 Gm.) before proceeding with surgery.

Atropine given preoperatively helps diminish the increased laryngeal reflexes (laryngeal spasm and coughing) and to prevent spastic adduction of the vocal cords. Excessive premedication with other barbiturates should be avoided. Morphine adds to depression of respiration and should be avoided if possible.

Signs of anesthesia: (1) Thick speech; (2) slowing of respiration; (3) loss of eyelid, eyelash, and conjunctival reflexes.

During induction there is an initial fall in blood pressure but it soon returns to normal. Complete relaxation is not necessary. The most reliable sign is the respiration of the patient. Respiration in deep anesthesia is shallow and abdominal with slight to moderate cyanosis. Some consider it advisable to administer oxygen throughout the operation. Thiopental is rapidly destroyed in the body so that it must be repeated as needed to maintain adequate anesthesia.

Contraindications. Since thiopental sodium is detoxified in the liver it should not be administered to patients with any hepatic disease or diabetes. It is contraindicated for patients suffering from shock, pulmonary disease, asthma, and cardiovascular ailments. It is not tolerated well by children or old, debilitated individuals. The drug should not be given to those afflicted with tumors or swellings of the neck or floor of the mouth, which might obstruct respiration.

Toxicity. When injected into the circulatory system too rapidly, thiopental sodium will produce marked respiratory depression culminating in respiratory failure. The blood pressure falls rapidly to shock levels. There is direct depression of the vasomotor centers and inhibition of smooth muscle tone. Signs of asphyxia are evident. The heart continues to function for several minutes after respiration ceases; pulse is weak and rapid. Resuscitation with oxygen under pressure should be instituted and respiratory and central stimulants given (pentylenetetrazol, U. S. P. (metrazol), picrotoxin, caffeine and sodium benzoate).

Local irritation. Sloughing of tissue may occur at the site of injection if the alkaline solution escapes into the subcutaneous tissue. If this occurs, infiltration of the site of injection with 1% procaine hydrochloride in isotonic sodium chloride has been suggested, presumably as a buffer.

Dosage forms. *Ampuls,* 0.5 Gm. and 1 Gm.; and 5 Gm. multiple dose ampul.

Chapter 4.

LOCAL ANESTHETICS

Drugs which on contact in safe concentrations temporarily abolish the excitability of nerve fibres are used as local anesthetics. There are many such drugs. They differ in penetration and toxicity as well as in potency and duration of effect. With any, an effective *concentration* must be in contact with the nerve to be numbed. Sensory nerve fibres are more sensitive than motor fibres because the sensory fibres are smaller and the myelin sheathes thinner.

POTENTIATION OF ANESTHETIC EFFECT AND REDUCTION OF TOXIC EFFECT

Alkalinization ($NaHCO_3$) increases the potency two- to four-fold, because the free bases penetrate more easily than do the salts. Vasoconstriction increases the effectiveness of local anesthetics by slowing the rate of absorption into the circulation, thereby facilitating the maintenance of an adequate local concentration of the drug. These two factors are clinically important since they improve the therapeutic safety ratio $\left(\frac{\text{therapeutic dose}}{\text{toxic dose}}\right)$. All local anesthetics are toxic, and hence the anesthetist should endeavor to obtain the optimum effect with the least amount of the least toxic drug. (Technique of administration is often as important as the pharmacologic considerations: e. g., proximity of the drug to the nerve; anesthetization of one nerve trunk vs. several branches; waiting for anesthetic effect.) Premedication with morphine or a barbiturate not only allays anxiety but reduces certain toxic effects.

TOXICITY

The symptoms of the toxic effects of local anesthetics and of the "alarm reaction" are similar and should not be confused. The toxic effects of local anesthetics are due mainly to their CNS and cardiovascular action—anxiety, fainting, pallor, dyspnoea, convulsions, apnea, death. With smaller doses CNS stimulation may precede the depression. The best treatment is prevention. Toxic effects are a function of dosage and absorption; therapeutic effects relate more to the *concentration* of the drug in contact with the nerve. Precaution should be taken to avoid confusion of agents and concentrations.

TREATMENT OF POISONING

If the drug was taken orally, give chemical antidote (tannic acid, 2 Gm. in glass of water; or strong tea; or iodine, 2 cc. of tincture; or hydrogen peroxide solution, 4 cc.; or potassium permanganate, 1:10,000.) Evacuate by stomach tube. Give pentobarbital sodium, 0.1 Gm. to 0.2 Gm. intravenously if necessary. If the drug was injected, check absorption by ligation if possible; pentobarbital sodium intravenously; artificial respiration is the most effective treatment.

Soluble local anesthetics. Some are suitable for injection only (e. g., procaine), some for surface anesthesia only (e. g., cocaine), and others for both injection and surface anesthesia (e. g., tetracaine).

Slightly soluble local anesthetics. Suitable only for surface anesthesia of wounds and mucous surfaces. Due to slow absorption, their effect is more prolonged but not as complete as with the soluble drugs (e. g., ethyl aminobenzoate).

Volatile local anesthetics. These freeze the skin by rapid evaporation (e. g., ethyl chloride).

SOLUBLE LOCAL ANESTHETICS

COCAINE HYDROCHLORIDE, U. S. P. Salt of an alkaloid obtained from the leaves of Erythroxylon Coca. Soluble in water (1 in 0.5) and in alcohol (1 in 3.5).

This drug is a very effective but very dangerous *surface* anesthetic. It should not be injected under the skin or mucous membranes. Urethral injection is dangerous. Cocaine is useful for anesthesia of the surface of the eye and for the nose, where it also has a vasoconstrictor effect, but it is being replaced by less toxic topical anesthetics. The repetitious use of cocaine may lead to addiction.

LIDOCAINE HYDROCHLORIDE, N. N. R. (Xylocaine Hydrochloride). As a local anesthetic lidocaine produces more prompt, intense, and extensive anesthesia than an equal concentration of procaine hydrochloride. (Approximately twice as potent as procaine.) It may be used in combination with epinephrine, or without it, if vasopressor drugs are contraindicated.

Uses. Lidocaine is useful for infiltration and block anesthesia in dental, oral, and general surgical procedures. It has been employed for continuous caudal, peridural, and spinal (subarachnoid) anesthesia with promising results, but until its toxic potentialities have been more completely explored, it should be used only for the less hazardous low caudal anesthesia. By all the above mentioned routes, however, lidocaine provides adequate anesthesia with a lower dosage and less fall in blood pressure than the better known agents (procaine and tetracaine).

Toxicity. A 1% solution of lidocaine is 40 percent more toxic and a 2% solution is 50% more toxic than an equal concentration of procaine. A 0.5% solution has the same toxicity as an equal concentration of procaine.

Systemic side reactions and local irritant effects are rare. Nausea, vomiting, muscular twitching, and chilling have been observed after ordinary doses.

Dosage. The maximum dose is the same as for procaine (0.5 Gm. in 24 hours). When lidocaine is employed without epinephrine the minimum effective dosage should be used.

For infiltration, 0.5% solution with epinephrine 1:100,000. If the operation requires more than 100 cc. (thoracoplasty) a 0.25% solution should be used. For block anesthesia a 1 to 2% solution is employed. Some odontologic procedures require a 2% solution with epinephrine 1:50,000.

PROCAINE HYDROCHLORIDE, U. S. P. (amino-benzoyl-diethyl-amino-ethanol hydrochloride). White crystals, freely soluble in water (1 in 1). Soluble in alcohol (1 in 30).

Procaine hydrochloride, the least toxic of all local anesthetics, is probably the most important drug in this group. Like all the synthetic local anesthetics it produces no euphoria and a dilation has not been reported.

or the exposed pulps of the teeth. By hypodermic injection procaine hydrochloride is used to produce infiltration and block anesthesia (paravertebral, spinal, and epidural).

In clinical use the drug is almost always administered in combination with a vasoconstrictor such as epinephrine. This slows the rate of absorption, thus prolonging the local anesthetic effect and reducing the chances of toxic systemic reactions.

Toxicity and incompatibility. (For toxicity see introductory statements to this section.)

The use of procaine hydrochloride and other local anesthetics derived from para-amino-benzoic acid inhibits the action of sulfonamides. Conversely, the sulfonamides antagonize the effect of procaine hydrochloride.

Dosage. One to two percent solutions are most commonly used, with epinephrine, 1:50,000 or 1:25,000. For infiltration, 0.25% to 0.5%. A total injection of 0.5 grams of procaine hydrochloride (50 cc. of a 1% solution) during the course of a surgical procedure is a conservative amount. In oral surgery a 2 percent solution usually is employed, but the total volume injected rarely exceeds 10 cc.

Dosage forms:

Ampuls: 1% and 2% solution, in various sizes. Crystals, for spinal anesthesia, 50, 100, 150, 200, 500 mg.

Tablets, hypo: 20, 50, 60, 80, 100 mg. with and without epinephrine.

TETRACAINE HYDROCHLORIDE, U. S. P. (Pontocaine Hydrochloride). White, odorless, crystalline powder, very soluble in water, soluble in alcohol. Aqueous solutions are stable and can be sterilized by brief boiling.

Actions and uses. Potent local anesthetic, about 15 times as effective as cocaine. Superior to procaine as surface anesthetic because of better penetration of intact mucous membranes. It is an effective eye anesthetic. It is nonmydriatic, noncycloplegic, and does not raise intraocular pressure. As a spinal anesthetic its action is prolonged up to 3 hours in duration. For use particularly as surface anesthetic for the eye, nose, and throat, and in spinal anesthesia.

Dosage:

Ophthalmic: 0.5% solution and ointment.

Nose and throat; dental: 1% or 2% solution diluted with equal parts of epinephrine solution (1:1000).

Spinal anesthesia: 1% solution using 1 cc. to 2 cc. (10 mg. to 20 mg.).

Continuous caudal anesthesia: 0.15% solution. Initial injection of 30 cc., then 10 to 20 cc. every 40 to 90 min. Usually a total of 100 cc. is sufficient.

Dosage forms:

Pontocaine solution, 0.5%, 2% for topical use.

Ampuls of powder, for spinal anesthesia, 10 mg. and 20 mg.

Ampuls, solution, 1% 2 cc.

Ophthalmic Ointment, 0.5%.

Tablets, 0.1 Gm., for making solutions for topical use.

ETHYL AMINOBENZOATE, U. S. P. (Benzocaine); Ethyl-p-aminobenzoat Soluble in alcohol (1 in 5); sparingly soluble in expressed almond oil or olive o (1 in 30 to 50).

Actions and uses. Useful as a local anesthetic for painful wounds, burn ulcers, etc., hemorrhoids, pharyngitis, tonsillitis, and following dental operation

Used externally in ointment form, or suppositories, 5%; in dusting powde 10% to 20%, or undiluted; troches, 30 mg. (½ gr.).

VOLATILE LOCAL ANESTHETICS

ETHYL CHLORIDE, U. S. P. Volatile, colorless liquid, which freezes the ski by rapid evaporation. The vapor is very inflammable.

Actions and uses. Used principally for local anesthesia in inflamed area where injection anesthesia is not feasible. Its use is impractical for other pu poses and it makes incision more difficult.

It is used for induction of general anesthesia by open mask ether anesthesi and should be so used only by trained anesthetists.

Dosage form. Special spray *bottles* or *tubes.*

AGENT FOR NERVE BLOCK

ALCOHOL, U. S. P. In the management of severe and chronic pain of such distribution as to be relievable by nerve block, alcohol may be injected aroun the nerve or ganglia controlling sensation from the painful area. The effec may last for several months.

LOCAL ANTI-INFECTIVES

Confusion exists in this field chiefly because laboratory tests are still inadequate and due to the promotion and acceptance of misinformation as factual. Pathogenic organisms vary in their susceptibility to anti-infectives; spores present most difficult problems; serum, blood, and pus interfere; and few anti-infectives measure up to claims or definitions. The terms germicide, antiseptic, and disinfectant have strict meanings for which few, if any, local anti-infectives can truly qualify. Yet, withal, clinical experience indicates that their use has some rational basis.

Preliminary, thorough cleansing of the area is essential for obtaining satisfactory effect of local anti-infectives. Basically, alcohol and iodine are the only substantially effective agents in this class. Other drugs are included only because iodine and alcohol have somewhat limited ranges of usefulness. Mercurials are so greatly overrated that they are not included.

With respect to instruments (thermometers, knives, etc.) which cannot tolerate heat sterilization, various chemicals have been used to prevent or control contamination. These chemicals, incorrectly described as agents used for "cold sterilization," reduce the number of bacteria. As far as can be told, spores are unaffected. None accomplish true sterilization and the term "cold sterilization" in this sense therefore is a misnomer. All that can be done is to select the best and at the same time recognize the limitations inherent in this method of decontamination. Such a compromise seems unavoidable at this time.

The following summarizes a suggested approach to the use of local anti-infectives:

1. **For clean wounds and superficial cuts.** Cleansing of the area with soap and water, followed by 70% alcohol. Iodine tincture may be used, but dressings, if used, should allow access of air.

2. **For dirty wounds.** Cleansing with soap and water, followed by flushing with isotonic sodium chloride solution and then, if indicated, chloroazodin (azochloramid) solution.

3. **Preoperative skin preparation.** Soap and water scrubbing followed by iodine tincture carefully removed, after drying, with 70% alcohol.

Where iodine tincture is contra-indicated, 1:1,000 benzalkonium chloride (Zephiran) solution may be used.

4. **Preoperative hand scrub.** Hexachlorophene in suitable detergent solution.

5. **Mucous membranes.** Soap and water cleansing, followed by 1:13,200 chloroazodin, or 1:2,000 to 1:10,000 benzalkonium chloride (zephiran). Soap must be completely removed or effect of the benzalkonium chloride will be nullified.

6. **Instruments harmed by heat.** Careful soap and water scrub followed by immersion in a formaldehyde alcohol solution.

There follows a listing and description of the local anti-infective drugs included. **Anti-infective drugs used in dermatologic practice** are described in the chapter dealing with dermatologic drugs.

ALCOHOL, U. S. P. (Ethyl Alcohol, Ethanol). 95% by volume (92.4% by weight) of ethyl alcohol. Boils at 78°; flammable.

Alcohol precipitates proteins and has a high affinity for water. These actions enable alcohol to kill bacteria (nonsporulating) on relatively brief contact (5 minutes) in suitable concentrations. The effective range is 50 to 90% (by weight); the optimum bactericidal strength is about 70%. Scrubbing of the surface insures better exposure of bacteria to the alcohol. Isopropyl alcohol is as effective as ethyl alcohol, but has greater defatting action on the skin.

ISOPROPYL ALCOHOL, N. F. Not less than 99% by weight of isopropyl alcohol. Flammable. See "Alcohol" for uses.

ACETONE

ACETONE, N. F. Contains not less than 99% of acetone. Flammable.

Action and uses. For skin preparation prior to dermal insertion procedure. Greater cleansing and fat solvent effect than alcohol. Especially for use prior to smallpox vaccination.

ANTIBIOTICS

Two antibiotics, aureomycin and bacitracin, are included among the local anti-infective drugs because as yet there has been little or no evidence of sensitivity and local reaction from their use. This is in contradistinction to the undesirable side effects of local therapy with penicillin, which has not been included for local use.

AUREOMYCIN HYDROCHLORIDE, U. S. P. (See ch. 6, "Antibiotics and Sulfonamides," for further description.)

Actions and uses. For treatment of local infections caused by susceptible organisms.

Dosage and Dosage forms:

Ointment, 3%.

Ointment, Ophthalmic, 0.1%.

Ophthalmic solution: Package of 25 mg. of aureomycin hydrochloride (with sodium chloride and sodium borate) to which 5 cc. of distilled water is added to effect a 0.5% solution. One or 2 drops every 2 hours in affected eye. Solution is stable for 2 days only, if refrigerated.

BACITRACIN. Antibiotic substance obtained from *Bacillus subtilis.* Light tan powder freely soluble in water. Solutions remain stable for 3 weeks if stored in refrigerator at 5° to 10° C. Stable in dry form for at least 18 months at room temperature.

Actions and uses. Specifically effective against alcaligenes faecalis, endamoeba histolytica, neissoria catarrhalis, neisseria intracellularis, sarcina flava, staph. alb., staph. aur., strept. agalactiae, strept. dysgalactiae, strept. faecalis, strept. hemolyticus (D), strept. mastitidis, strept. viridans. May be considered in infections caused by: aerobact. aerogenes, aerobacter cloacae, bac. anthracis, bac. mycoides, bac. subtilis, chromobact. violaceum, escherichia communior. Effective by *local infiltration* in pyogenic lesions such as furuncle, deep abscess, infected operative wounds, carbuncle, infected sebaceous cyst. Low allergenicity.

Ophthalmic ointment is indicated in infections due to bacitracin susceptible

Bacitracin solution, (0.2 cc. to 5 cc. containing 500 units per cc. in sterile isotonic sodium chloride solution or in 1% procaine hydrochloride solution) injected into base of pyogenic lesion.

Dosage forms:

Bacitracin *Powder*, 50,000 unit vial.

Bacitracin *Ointment*, 500 units per gram.

Bacitracin *Ophthalmic Ointment*, 500 units per gram.

CHLOROAZODIN

CHLOROAZODIN, U.S.P. (Azochloramid). Chemically, a,a'-Azo-bis (chloroformamidine) contains 37.5 to 39.5% active chlorine. Very slightly soluble in water; sparingly in alcohol; slightly in glycerin and in glyceryl triacetate. *Sensitive to light.*

Actions and uses. Has bactericidal action similar to that of other chlorine-containing preparations (e. g., sodium hypochlorite). Has the advantage of stability in contrast to the quickly dissipated effect of sodium hypochlorite solutions. Therefore its effect is more prolonged. Not affected appreciably by pus and organic matter. Action on microorganisms is nonselective.

Aqueous solutions are used for wound irrigation, cavity instillation and for application to mucous membranes. Solution in glyceryl triacetate (chloroazodin solution, U. S. P.) is used as wound dressing and as packing in infected cavities, in pus pockets, and deep wounds.

Dosage. 1:3,300 buffered aqueous saline solution (pH 7.4); greater dilutions, up to 1:13,200 for mucous membranes. For dressings and packing, 1:500 in glyceryl triacetate (triacetin) applied to gauze, does not dry out or stick to wound. A 1:125 solution in glyceryl triacetate, diluted 1 part with 19 parts of a vegetable oil gives a 1:2,000 dilution suitable for application to mucous membranes of vagina, colon, rectum.

Dosage forms. *Powder*, for saline mixture: 3.17% chloroazodin, with buffering salt mixture of 89.50% sodium chloride, 0.95% monopotassium phosphate, 6.32% anhydrous sodium phosphate. In bottles of 35.93 Gm. for preparation of 1 gallon of 1:3,300 aqueous solution.

Chloroazodin *Solution*, U. S. P. 1:500 solution of chloroazodin (azochloramid) in glyceryl triacetate (triacetin).

Strong *Solution* Chloroazodin (Azochloramid) in Triacetin (1:125).

CRESOL

SAPONATED CRESOL SOLUTION, N. F. Cresol, 50% dissolved in vegetable oil soap.

Actions and uses. Germicidal power about twice that of phenol. Should always be diluted before use—maximum concentration, 5% of the saponated solution (1 part solution and 19 parts water). Principally used for disinfecting inanimate objects (2% dilution is adequate). May be used on skin in 1% dilution; mucous membranes, 0.25 to 0.5% dilution; 1% dilution to kill bacterial cultures.

FORMALDEHYDE SOLUTION, N. F. 37% formaldehyde with variable amounts of methanol to prevent polymerization.

Actions and uses. Formula containing formaldehyde sol., 8%, isopropyl alcohol, 50%, methanol, 3%, sodium nitrite, 1%, distilled water to 100% for storage of instruments which cannot be sterilized by heat.

HEXACHLOROPHENE

HEXACHLOROPHENE. White powder, relatively insoluble in water; soluble in alcohol, acetone, dilute alkali.

Action and uses. Highly bacteriostatic agent, having chlorine-phenol activity. When added to soap and other detergents, in 2 to 3% concentration, the combination markedly reduces the bacterial flora on the skin after 1- to 3-minute scrub. Continued use leaves sufficient residual to keep the bacterial count at a significantly lower level than otherwise. Use of non-hexachlorophene detergents dissipates this effect. Best effect is obtained by continued use; single, irregular washings are not too effective. Used for preoperative skin preparation as well as surgical scrub. Possible toxic effect contraindicates use in open wounds.

IODINE

IODINE, U. S. P. Grayish black plates with metallic luster and characteristic odor. Although slightly soluble in water (1:2,950) dissolves readily in the presence of an iodide salt; soluble in alcohol (1:13).

Actions and uses. Iodine is an effective antiseptic even in concentrations as low as 0.1%. Also an effective fungicide. As Iodine Tincture, U. S. P., it is used for preoperative preparation and general disinfection of the skin. This tincture, containing 2% of iodine, sodium iodide to aid in solution of the iodine and to enhance stability, and approximately 47% of alcohol, is an improvement over the earlier U. S. P. tincture which contained 7% of iodine and 82% of alcohol. A 1% tincture is about as effective as 2%.

Aqueous solutions of iodine penetrate unabraded skin well but do not dry as quickly as the tincture.

Iodine preparations are stable if stored in an all-glass container or a glass container having a closure resistant to iodine action.

To avoid tissue irritation, surfaces painted with iodine should not be covered.

Dosage form. Iodine *Tincture*, U. S. P.

SILVER

SILVER NITRATE, U. S. P. Colorless crystals, very soluble in water (1:0.4); soluble in alcohol (1:30).

Actions and uses. Astringent, antiseptic, caustic—depending on strength of solution and duration of application. Antiseptic action is due to liberation of silver ions which precipitate the protein of the bacterial protoplasm. Caustic action is limited by the formation of protein precipitates in the tissues.

Ophthalmia neonatorum: 1% solution instilled into conjunctival sac.

Infected ulcers in mouth: 10% solution carefully applied with pledget of cotton.

(See chapters on drugs used in dental practice and in dermatologic practice for other uses and preparations.)

Caution in use. In prophylaxis of ophthalmia neonatorum, use with caution to prevent cauterization of the cornea. After cleansing eyelids, one drop of 1% solution should be instilled in each eye.

SURFACE ACTIVE AGENT

BENZALKONIUM CHLORIDE, U. S. P. (Zephiran Chloride). Mixture of alkyl-dimethyl-benzylammonium chlorides. White or yellowish white, amorphous powder, or gelatinous pieces. Aromatic odor, very bitter taste. Solutions are alkaline to litmus and foam strongly when shaken. Very soluble in water, alcohol, acetone.

Actions and uses. Surface disinfectant, pathogenic to many pathogenic non-sporulating bacteria and fungi after several minutes exposure. Solutions have low surface tension and have detergent, keratolytic, and emulsifying actions.

Presence of soaps (anionic detergents) neutralize the germicidal activity of benzalkonium chloride (cationic detergent), therefore soap cleansed areas should be thoroughly rinsed.

Preoperative disinfection of unbroken skin; treatment of superficial injuries and fungous infections: 1:1,000 solution or tincture.

Therapeutic disinfection of deep lacerations, storage of metallic instruments and rubber articles: 1:1,000 solution. (For instruments, 0.5% sodium nitrite is added to prevent rusting.)

Instillation and irrigation of the eye or vagina: 1:5,000 to 1:2,000 solution.

Irrigation of infected deep wounds: 1:3,000 solution.

Preoperative disinfection of mucous membrane and denuded skin: 1:10,000 to 1:2,000 solution.

Widely denuded surfaces: 1:10,000 to 1:5,000 solution.

Bladder and urethral irrigations: 1:20,000 solution.

Retention lavage of bladder: 1:40,000 solution.

Dosage forms. Concentrated solution, 12.8%, for preparing weaker solutions.

TRICHOMONACIDE

IODOCHLORHYDROXYQUIN, N. F. (Vioform). 5-chloro-7-iodo-8-hydroxy-quinoline. 38–41.5% iodine, 11.4–12.2% chlorine. Brownish yellow powder, slight characteristic odor. Insoluble in water or alcohol.

Actions and uses. The agents used in the treatment of trichomonas vaginitis are variable in response from patient to patient. Iodochlorhydroxyquin has been selected because it has had a fair degree of success. Used as suppository containing 250 mg. of the drug, together with 25 mg. lactic acid and 100 mg. boric acid. (See section on drugs used in dermatologic practice, for other local uses.)

Dosage. 1 or 2 suppositories (depending on extent of invasion) each night, preceded by vinegar douche (2 or 3 tablespoonfuls to quart warm water), for 6 weeks, through the menstrual cycle, except that the douche is omitted during menstrual period.

Dosage form. *Suppository*

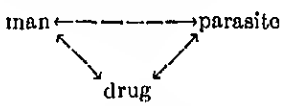
Chapter 6.

SYSTEMIC ANTI-INFECTIVES

Aati-Infective agents given internally are included under this major classification. For convenience, these systemic anti-infectives have been grouped as follows:

Anthelmintics, Antibacterial drugs, Antibiotics and Sulfonamides, and Antiprotozoan drugs

The selection and use of these drugs are bound up in a trilogy of actions and interactions which may be depicted as follows:



The ideal anti-Infective drug destroys the parasite without harm to man, the host. The criterion of selection is that of closest approach to this ideal.

ANTHELMINTICS

Anthelmintics are used to rid patients of intestinal and tissue parasites. Presently available anthelmintics stun rather than kill parasites, require that definite precautions be taken to safeguard the health of the host, tend to be more effective against certain parasites than others, and require that provision be made for evacuating the intoxicated parasites before they recover. Accordingly, the procedure of divorcing parasites from host involves provisions for: (1) definitive diagnosis; (2) maximum exposure of the parasite to the drug through prior removal of protective mucus and feces (by fasting and purgatives) without unduly weakening patient or facilitating absorption of the anthelmintic; (3) administration of the vermicide considered to be most effective against the particular parasite, *if clinical judgment indicates that the patient will tolerate it;* if not, compromise; (4) expelling the parasites and anthelmintic with a cathartic which correlates the locus of the parasites with *site and time of action of the cathartic, and which will* not facilitate absorption of the vermicide; (5) sanitary disposition of evacuated material; and (6) checking the patient for effectiveness of the procedure.

While any cathartic is a vermifuge, magnesium salts have certain advantages, because oily cathartics often facilitate absorption of the anthelmintic and therefore tend to increase the toxicity for the patient.

1. *Nemathelminthes (Nematodes)*	*Anthelmintic*
Ankylostoma duodenale Necator americanus (hookworm)	Tetrachloroethylene. (Watch and treat for accompanying roundworm infestation.)
Ascaris lumbricoides (roundworm)	Hexylresorcinol
Trichocephalus trichiuris (whipworm)	Hexylresorcinol
Strongyloides stercoralis	Methylrosanilino Chloride
Oxyuris vermicularis (pinworm)	Methylros. Chlor., Hexylresorcinol
Trichinella spiralis	(?)
Filariae	Antimony Potassium Tartrate
2. *Platyhelminthes*	
A. Tapeworms (cestodes)	
Hymenolepis nana (dwarf tapeworm)	Hexylresorcinol
Taenia saginata (beef tapeworm)	Aspidium Oleores., quinacrine
Taenia solium (pork tapeworm)	Aspidium Oleores., quinacrine
Diphyllobothrium latum (fish tapeworm)	Aspidium Oleores., quinacrine
B. Flukes (trematodes)	
Schistosoma haematobium, mansoni, or japonicum	Antimony Potassium Tartrate
Clonorchis sinensis	Methylrosaniline Chlor.
Fasciolopsis buski	Tetrachloroethylene
Heterophyes heterophyes	Tetrachloroethylene
Metagonimus yokogarvai	Tetrachloroethylene
Gastrodiscoides hominis	Tetrachloroethylene

ANTHELMINTIC DRUGS

ANTIMONY POTASSIUM TARTRATE, U. S. P. Colorless, odorless, transparent crystals or white powder. The crystals effloresce on exposure. Solutions are acid.

Actions and uses. Treatment of schistosomiasis, filariasis; also has been used against granuloma venereum.

Dosage. 0.03 to 0.12 Gm. (3 to 12 cc. of freshly prepared 1% solution intravenously, slowly). *Caution:* Best time for administration is 2 to 3 hours after a light meal. Extravasation of the solution should be avoided. Patient should remain in bed for an hour. Injections should be terminated if symptoms arise. Starting with small amounts given on alternative days, gradually work dosage up to 120 mg. or a smaller maximally tolerated amount, and repeat this about 15 times.

Dosage forms. Antimony Potassium Tartrate, *ampuls*, 1%, 5 cc.

ASPIDIUM OLEORESIN, U. S. P. Thick, dark green liquid. Effective against tapeworm, especially Diphyllobothrium latum. *Toxic effects:* If absorption occurs (which is not usual) vomiting and purging, weakness, spasms in extremities, convulsions, stupor deepening into coma, collapse; occasionally disturbance of sight, hearing; sometimes permanent blindness.

Dosage. Adult: 4 Gm. in two 2-gram doses, 1 hour apart. Child: 0.5 Gm. per

[1] The classification of the helminths only is taken from Goodman, Lewis and Gilman, "Text-book of Therapeutics."

before. Magnesium sulfate given 2 to 3 hours after second dose of drug; enema given 2 hours after cathartic, to remove dislodged head of worm. Should it be necessary to repeat treatment, wait for 2 or 3 weeks.

Dosage form. *Capsule*, 1 Gm.

HEXYLRESORCINOL, U. S. P. Pale yellow, crystalline substance soluble 1:2,000 in water and freely soluble in organic solvents. *It is a local irritant*, damaging tissue on contact of drug or concentrated solution.

Actions and uses. Most versatile anthelmintic; effective against hookworm, roundworm, pinworm, dwarf tapeworm, whipworm.

Toxic effects. Avoid contact with tissue (mouth ulceration may result); limited absorption makes for low toxicity.

Dosage. Children, under 6 yrs, 0.6 Gm. Children, 6 to 10 years, 0.8 Gm. Adults, 1 Gm. Given in hard gelatin pill, to be swallowed *without chewing*. Usual dietary and cathartic regimen.

Dosage forms. *Hard gelatin pill*, 0.1 Gm., 0.2 Gm.

METHYLROSANILINE CHLORIDE, U. S. P. (Gentian Violet). *Dark greenish* powder, soluble 1:30 water, 1:10 alcohol, 1:15 glycerin.

Actions and uses. Most effective anthelmintic known against pinworm; also of value against strongyloides and clonorchis sinensis (liver fluke). It is bactericidal to gram-positive organisms; very effective against B. diphtherias. B. pyocyaneus, and the causative organisms of Vincent's angina. Gram-negative organisms little affected. Good superficial antiseptic for mucous membrane, ulcers, infected wounds, and burns. Also used in treatment of cystitis, urethritis, infectious eczematoid dermatitis, furunculosis, pruritus ani, pruritus vulvae.

Dosage. *Oxyuriasis*—30 mg. (*enteric coated tablets*) three times daily before meals; treatment continued for 10 days. *Strongyloidosis*—60 mg. (enteric coated tablets) three times daily before meals until total of 3.3 Gm. taken; if no effect, 2.5 cc. of 1% solution may be instilled by tube directly into duodenum. *Clonorchis sinensis* (liver fluke)—60 mg. (enteric coated tablets) three times daily before meals for 1 month.

Pediatric Dosage. 3 mg. three times daily for each year of age for the same period of time.

Note: In mixed infestation together with ascaris (roundworm) drug may cause migration of roundworm, resulting in intestinal obstruction; therefore prior elimination of roundworms necessary.

For local application as antiseptic: 0.1% to 1% solution; 1:10,000 sol. for instillation into closed cavities.

Dosage forms. *Tablet* (enteric coated), 9 mg., 30 mg.; *solution*, 1%.

QUINACRINE HYDROCHLORIDE, U. S. P. (Atabrine Dihydrochloride). Quinacrine has been found to be fairly effective against the large tapeworms (Taenia saginata, Taenia solium), and probably Diphyllobothrium latum. After usual preparation, the adult patient is given 0.6 to 0.8 Gm. (two tablets every five minutes with one glassful water along with 0.6 Gm. sodium bicarbonate). One hour after the last dose, give saline cathartic. For details on toxicity, refer to description of quinacrine under Antiprotozoan Drugs (p. 59). Pregnancy is considered to be a specific contraindication.

Dosage form. *Tablets*, 0.1 Gm.

STIBAMINE GLUCOSIDE, N. N. R. (Neostam Stibamine Glucoside). This

maniasis (kala-azar) than the trivalent form. It is said to be less effective than trivalent antimony (antimony potassium tartrate) against schistosomiasis and filariasis. It may be injected intramuscularly. It may cause vomiting and diarrhea. Hepatitis has occurred. It is contraindicated in liver or kidney disease.

Dosage. 0.1 Gm. per 100 lb. of body weight, fresh 4% solution, maximum dose 0.2 Gm. Give on alternate days for a total dose of not more than 3 Gm. per 100 lb. of body weight. In sensitive patients, start with 0.05 Gm. per 100 lb. and increase doses as tolerance develops.

Dosage form. Neostam stibamine glucoside, N. N. R., *ampuls* (powder for solution), 0.1 Gm., 0.5 Gm.

TETRACHLOROETHYLENE, U. S. P. Colorless liquid, practically insoluble in water; readily soluble in alcohol and oils.

Actions and uses. Effective against hookworm, more so against ankylostoma duodenale than necator americanus. Limited value against oxyuriasis. Effective against flukes. In mixed infestations, eliminate roundworms first.

Toxicity. Narcotic effects with vertigo, emesis. Therapeutic doses cause no liver or kidney damage. On exposure tetrachloroethylene forms phosgene (do not use broken capsules).

Dosage. Adult—one to three 1 cc. capsules, patient in post-absorptive state; usual preliminary diet and cathartic. Children—0.2 cc. per year of age.

Dosage forms. *Capsule* U. S. P., 0.5 cc., 1 cc.

ANTIBACTERIAL DRUGS

"Antibacterial Drugs" includes those chemical agents used systemically to combat bacterial infection.

CALCIUM MANDELATE, U. S. P. White powder, tasteless, slightly soluble in water.

Actions and uses. The results obtained in treating urinary infection with a ketogenic diet led to the use of other acid-producing methods, such as administration of mandelic acid. Mandelic acid is not metabolized and in passing through the kidney creates a pH of 5 to 5.5 in the urine. Concentration of 0.25% to 1% of acid in the urine gives a pH of 5 to 5.7. This therapy often is successful when sulfonamides are ineffective or otherwise objectionable. Calcium mandelate is far more palatable and more stable than the acid. The calcium ion combines with bicarbonate in the duodenum, releasing mandelic acid.

Effective against E. coli, Aerobact. aerogenes, Strept. faecalis, Shigella, Pseudomonas, Salmonella, Alcaligenes, Proteus.

Toxicity. Nontoxic. Occasionally, nausea, diarrhea, hematuria (microscopic). Contraindicated in hepatic insufficiency.

Dosage. 3 Gm. every 4 hours after meals and at bedtime.

Dosage form. *Tablet*, 0.55 Gm. yielding 0.5 Gm. of mandelic acid.

METHENAMINE, U. S. P. Colorless, odorless, sweet, then bitter taste. Freely soluble in water (1:1.5).

Actions and uses. Potent urinary antiseptic act ng only in urinary infections resistant to

chloride or sodium biphosphate after meals. Tablets containing methenamine and the acidifying agent are irrational since simultaneous administration will cause release of formaldehyde in digestive tract; combination is also unstable in tablet form.

Dosage forms. *Tablets*, U. S. P., 0.3 Gm., 0.5 Gm.

p-AMINOSALICYLIC ACID, N. N. R. White or nearly white powder; odorless or slight acetone odor. Soluble 1:500 in water; 1:21 in alcohol; 1 Gm. dissolves in 10 cc. of 10% sodium bicarbonate solution.

Actions and uses. Effective against tubercle bacillus. Usually employed together with streptomycin therapy. May also be used alone in patients unable to tolerate streptomycin therapy or where the bacilli have become resistant to the latter. Easily absorbed and excreted.

Toxicity. Gastro-intestinal symptoms may be troublesome.

Dosage. Recommended daily dose 8–16 Gm. divided into four doses.

Dosage form. *Tablets*, N. N. R., 0.5 Gm.

SULFONAMIDES. See Chapter 6: "Antibiotics and Sulfonamides."

Sulfone Compounds

SULFOXONE SODIUM, N. N. R. (Diasone Sodium). Not less than 77% anhydrous disodium (sulfonylbis (p-phenyleneimino)) dimethanesulfinate. Pale yellow powder with characteristic odor; very soluble in water; very slightly soluble in alcohol.

Actions and uses. Treatment of Hansen's disease. Usually halts progress of lesions. Healing of mucous membrane lesions is earliest and most frequent sign of response, followed by improvement in skin lesions.

Toxicity. Commonest effect is a transient normocytic anemia. Drug is not stopped unless the anemia becomes severe. Recovery from the anemia usually between third and sixth week of therapy. Methemoglobinemia occurs in about half the patients, but drug is not withdrawn unless anoxemia is acute. Other effects: nausea, hematuria, drug rash, leukopenia.

Dosage. Adults:—Initial dose, 0.3 Gm. daily. If no symptoms of intolerance during first week, dose may be increased to 0.6 Gm. daily, continued for 2 or 3 weeks. If no symptoms of intolerance, may increase to 0.9 Gm. daily, continued for 6 months or more if no severe side effects. At least 6 months required to evaluate effect. Rest periods of 2 weeks every 2 months advised.

Children, 6 to 12 years—0.15 Gm. daily, initial, increasing to 0.6 Gm. at monthly intervals if no contraindication. *4 to 6 years*—maximum daily dose may be 0.45 Gm. *Younger children*—information not available.

Dosage forms. *Tablets*, 0.3 Gm., *enteric coated*. *Tablets*, 0.15 Gm.

Other agents used in Hansen's disease, not presently official or listed in N. N. R., are **Promin** (intravenous), **Promacetin, Sulfetrone.**

ANTIBIOTICS AND SULFONAMIDES

The advent of sulfonamide therapy, followed by the antibiotics, has introduced a number of agents effective against a wide range of infections. The following tabulation is intended to lend perspective as between infection and choice of drugs at this time. Where the advantages of one over another are clear cut, we have tried to so indicate. For example, although a number of antibiotics are effective

may be selected.

Type of infection or disease	Penicillin	Aureomycin	Terramycin	Chloramphenicol [1]	Dihyd. & streptomycin	Sulfonamide
Gram-positive organisms:						
B. Anthracis (Anthrax)	+	+	?	?	+	+
Clostridia (gas gangrene)	+	?	?	?	—	+-
Pneumococci	+++	++	+	—	+	+-
Staphylococci	+	++	+	—	+	+
Streptococci:						
Group A beta hemolytic	+++	++	+	+	+	+
Alpha hemolytic	+	+	+	+	+	?
Str. faecalis (Group D)	+	++	?	?	+	—
Gram-negative organisms:						
Bacilli:						
Aerobact. Aerogenes	—	+	+	+	+	+
Brucellae	—	+	+	+	—	—
E. Coli	—	+	+	+	+	+
Donovanie Granulomatis (Granuloma Inguin.)	—	+	+	+	+	+
H. Ducreyi (chancroid)	—	+	+	+	+	+
K. pneumoniae (Friedlaender bacillus)	—	+	+	+	+	+
H. influenzae	?	+	?	+	+	+
H. pertussis	—	+	+	+	+	+
P. pestis (Plague)	—	?	+	?	+	+
Proteus vulgaris	—	?	?	?	+	+
Pseudomonas Aerugenosa	—	—	?	?	+	+
Salmonellae (food)	—	?	?	?	—	—
Shigellae (bacillary dysentery)	—	+	+	+	—	+
P. Tularensis	—	+	+	+	++	?
E. Typhi	—	+	--	++	?	?
Cocci:						
Gonococci	+++	++	+	+	+	+
Meningococci	++	+	?	?	—	+-
Rickettsial (Typhus, Rocky Mt. Sp. Fever, Q Fever)	—	+	+	+	—	—
Spirochetal:						
Syphilis	++	+	+	+	—	—
Yews	++	?	+	?	—	—
Spirillum Minus	++	?	?	?	—	—
Virus: Trachoma	+	?	?	?	?	+
Virus-like:						
Lymphogran. Vener.	+	++	+	+	—	—
Psittacosis	+	++	+	+	—	—
Miscellaneous:						
Actinomyces	++	—	+	—	?	+
Dermatitis Herpetif.						SP
Primary atypical pneumonia	+	++	+	+	—	—
M. Tuberculosis	—	—	—	—	[2]+	—
Streptobacillus Moniliformis	—	?	?	?	+	—

KEY: +: effective (additional) + marks, where shown, indicate order of effectiveness in descending ord. of number of + marks); ?: effect doubtful or under investigation; —: indicates little or no effect; SI sulfapyridine.

[1] See text p. 54 as to cautious in use of chloramphenicol.
[2] With para-aminosalicylic acid.

agents. The pathogens against which the five antibiotics selected are effective are given in the table on page 52.

PENICILLIN. Derived from molds of the genus, *Penicillium.* Of the various forms isolated, penicillin G is the most readily available and is therapeutically effective for all penicillin-sensitive organisms. Crystalline penicillin is purer and more stable than the amorphous; available as sodium or potassium salt; stable up to 3 years in dry form without refrigeration; in solution below pH 6.0, stable for only 3 days at 8° to 14° C.; at or above pH 6.0, stable under refrigeration for minimum of 7 days.

One unit=penicillin activity contained in 0.6 microgram of the Food and Drug Administration standard; approximately equal to the original Oxford unit.

Uses. See table, page 52.

Toxicity. Essentially nontoxic, though delayed urticarial reactions occur. Locally, it may produce epidermal sensitivity in as many as 10% of patients.

Dosage. Penicillin by injection. Dosage and preparation used depend upon the type and locus of the infection and upon the individual patient. Blood level alone is not indicative of effective concentrations. Enough must be given to insure continuous effects at the locus, even if in excess of maximum needed. Small doses repeated frequently are no more effective than sufficiently large doses at longer intervals.

General dosage for severe infections. 300,000 to 600,000 units of penicillin in 24 hours.

Rapid absorption and excretion. Penicillin G Sodium (or Potassium) in sterile distilled water or isotonic sodium chloride solution, 10,000 units to 100,000 units per cc. Inject intramuscularly, preferably.

24-hour prolonged absorption and concentration. Penicillin procaine, 300,000 units per cc. in aqueous suspension.

48-hour or longer prolonged absorption and concentration. Penicillin Procaine in Oil Injection, U. S. P., 300,000 units per cc.

Penicillin orally. Requires 5 times the amount usually used for injection, given between meals.

Penicillin inhalation. It is questionable whether exposure of organisms to the drug is as thorough by this method. However, where there is good clinical reason to believe there is impairment of absorption by reason of interference with the circulation (e. g. bronchiectasis, lung abscess) inhalation therapy may be indicated. Usual dose is 25,000 to 50,000 units per cc. per day, by nebulization. Soluble tablets (50,000 u.) may be used to affect solution for this purpose.

AUREOMYCIN HYDROCHLORIDE, U. S. P. Yellow, crystalline antibiotic derived from *streptomyces aureofaciens.*

Uses. See table, page 52.

Toxicity. Relatively nontoxic but may produce nausea, vomiting, diarrhea, epigastric distress. These symptoms controllable by giving half the dosage every 3 hours or half the usual dosage every 6 hours for 1 or 2 doses then resuming regular dosage. Less tendency to gastric upset if capsule contents is dissolved in ½ glass of water.

for 1 or 2 days after temperature has returned to normal. In severe infections, if no response in 48 hours, dosage may be increased to 500 mg. every 3 hours.

Dosage forms:

Capsule, U. S. P., 50 mg., 250 mg.

Ampul, containing 100 mg.

Ophthalmic, 25 mg. of aureomycin hydrochloride powder together with 62.5 mg. sodium chloride and 25 mg. sodium borate. Dissolve in 5 cc. dist. water (see Local Anti-infectives).

Ointment, 3% (see Local Anti-infectives)

Ointment, ophthalmic, 1.0% (see Local Anti-Infectives).

CHLORAMPHENICOL, U. S. P. (Chloromycetin). Prepared either from cultures of *streptomycin venezuelae* or by chemical synthesis.

Uses. See table, page 52.

Toxicity. While this drug is ordinarily well tolerated, rapidly excreted, and destroyed, recent evidence implicates it as a causative agent of depression of hemopoiesis and formed blood elements in some patients. Of particular concern is the incidence of aplastic anemia following its use. For this reason, until such time as more is known it would seem reasonable to restrict its use to more serious clinical conditions for which chloramphenicol is clearly the agent of choice. At this time, therefore, it is recommended that chloramphenicol be reserved for use in patients with typhoid fever and those with infections which do not yield to other anti-infective agents or therapy and which on the basis of laboratory studies may be expected to respond to chloramphenicol.

As with sulfonamide therapy, frequent checks on red cells, white cells, and hemoglobin should be made during chloramphenicol therapy.

Dosage. *Average daily dose:* 25 mg. to 50 mg./Kg. body weight. *Infants and children:* 50 mg. to 100 mg./Kg. body weight as *daily dose.*

Dosage form. Capsule, U. S. P., 50 mg., 100 mg., 250 mg.

DIHYDROSTREPTOMYCIN, U. S. P., STREPTOMYCIN, U. S. P. Streptomycin is an antibiotic substance obtained from culture fluids of *Streptomyces griseus*; dihydrostreptomycin is its dihydro form.

These two drugs are described together in view of the present stage of indecision as to the relative advantages of each. Dihydrostreptomycin followed the introduction of streptomycin and was claimed to be less toxic and to have fewer undesirable side effects. There are differences of opinion as to the drug of choice. Pending the result of future clinical determinations, both drugs have been included. There seems to be some general agreement, however, that the sulfate salt of these drugs is better tolerated and is preferable to the hydrochloride.

Uses. See table, page 52.

Toxicity. Patients should be watched for vestibular and auditory (8th nerve) disturbances, renal irritation, shock, blood dyscrasia, skin eruptions, paresthesia about the face, tachycardia and hypotension, fever, flushing of skin, nausea, vomiting, headache, pain, and tenderness site of injection.

Dosage. Varies from patient to patient depending upon type and severity of infection. Acute fulminating infections: May require 2 to 4 Gm. daily, in divided doses every six hours. Less severe infections: 1 to 2 Gm. daily. Pulmonary tuberculosis: 1 Gm. two or three time weekly, usually given together with para-aminosalicylic acid (see page 51). Miliary and meningeal tuberculosis:

Dosage. The oral route is preferred but may be used locally, as in the ey
or intravenously in emergencies and where the oral route cannot be used becau
of the clinical condition of the patient. The daily oral dose should be about
mg./Kg. body weight or up to 50 mg./Kg. body weight in severe infections
nesses. The total daily dose should be administered in four equal portions
6-hour intervals.

Dosage forms. Capsules, 250 mg.

Sulfonamides

The first of the sulfonamides, sulfanilamide, was introduced in 1930 aft
discovery of its curative effect in streptococcic infections.

Pharmacologic action. *Inhibits bacterial growth. Sulfonamide compound*
basically consist of a benzene ring with one of the hydrogens replaced by
$—SO_2NH_2$ group, and the hydrogen in the para position replaced by an amin
($—NH_2$) group. It has been postulated that the presence of an adequate amoun
of para-aminobenzene-sulfonamide competes with the similar substance, para
aminobenzoic acid essential to the growth of many bacteria. The para-amin
benzoic acid thus is displaced and bacterial growth inhibited. An excess of th
sulfonamide drug must be present, and therefore vigorous dosage is required.

Therapeutic efficacy is affected by (1) *Acetylation*, occurring mainly in th
liver; reduces therapeutic effect. Except for sulfadiazine, the acetylated form
less soluble than the free drug, thus contributing to formation of renal concretion
(2) *Plasma protein binding of the drug.* It is reported that this binding to plasm
protein does not necessarily inactivate the drug since it is gradually released.

Toxicity. Worst side action is *agranulocytosis*, which fortunately occurs rarely
Sensitization, however, is fairly common. (*Sulfathiazole has been deleted* by th
Council on Pharmacy and Chemistry of the A. M. A. because of this.) *Toxi
phenomena vary* from patient to patient and from drug to drug. *Reaction
include* nausea, vomiting, headache, fever, rash, hematuria (especially from cryst
concretions). *Dangerous reactions include* hepatitis, anemia, extensive rash
hemoglobinuria, uremia, granulocytopenia. These may appear suddenly.

Precautions. The ever-present possibility of serious damage warrants frequen
checks on red and white blood cells, hemoglobin content, icteric index. *Photo
sensitizing* effect of the drug warrants avoiding exposure to sunlight or to ultra
violet therapy.

Sulfonamide therapy. There is theoretical advantage in a mixture of equa
parts of three different sulfonamides. There is reason to believe that renal effect
are sufficiently individual that each component is treated separately and conse
quently with less danger of crystallization than with full clinical doses of one of th
components. The therapeutic effects of a mixture are thought to be additive
Nonetheless, the fluid intake with either a single sulfonamide or a mixture should
be enough to assure a 24-hour urine volume of at least 2 liters. Concomitan
alkali therapy is considered necessary when using a single drug, but may not be
as important with a mixture. The best mixture seems to be that containing equa

Two other sulfonamides are included: succinylsulfathiazole for use in bacillary dysentery; and sulfapyridine, which many consider to be the specific against dermatitis herpetiformis.

SULFADIAZINE, U. S. P. White or slightly yellow powder. Odorless, or nearly so; stable in air; slowly darkens on exposure to light. Soluble 1:13,000 in water; sparingly soluble in alcohol; freely soluble in dilute mineral acids and in solutions of potassium and of sodium hydroxide.

Actions and uses. See table, page 52.

Dosage. See below under "Meth-Dia-Mer-Sulfonamides."

Dosage form. *Tablets*, U. S. P., 0.5 Gm.

METH-DIA-MER-SULFONAMIDES, N. N. R. In 0.5 Gm. tablet, or in liquid suspension. Each tablet or each 4 cc. of suspension contains equal parts of sulfadiazine, sulfamerazine, and sulfamethazine.

Sulfadiazine, U. S. P. is p-amino-N-2 pyrimidyl benzene sulfonamide.

Sulfamerazine, U. S. P. is the methyl derivative of sulfadiazine.

Sulfamethazine, N. N. R. is the dimethyl derivative of sulfadiazine and the methyl derivative of sulfamerazine.

Uses. Sulfonamides are effective in treatment of many infections. (See table, page 52.

Dosage. Initial dose, 0.05 to 0.1 Gm. per kg. body weight, followed by 1 Gm. every 4 to 6 hours until temperature is normal for 72 hours. Administer fluids to maintain 24-hour urine output exceeding 2,000 cc. About 2 days required to attain optimal therapeutic effect (blood level 10 to 15 mg. percent).

Dosage forms. *Tablet*, 0.5 Gm.; *Suspension*, 0.5 Gm. per 4 cc.

SUCCINYLSULFATHIAZOLE, U. S. P. 2-(p-succinylaminobenzene sulfonamido) thiazole monohydrate.

Uses. Bacillary dysentery; preoperative and postoperative use in patients undergoing intestinal surgery. Is poorly absorbed and has low toxicity.

Dosage. Preoperative—initial, 0.25 Gm. per kg. body weight, followed by 0.25 Gm. per kg. daily in 6 equal portions at 4-hour intervals. Postoperative—0.25 Gm. per kg. daily for 1 or 2 weeks, as soon as patient is able to take fluid; same dosage for treatment of bacillary dysentery, until temperature has been normal for at least 2 days and stool cultures negative.

Dosage form. *Tablet*, U. S. P., 0.5 Gm.

SULFAPYRIDINE, N. F. For the treatment of dermatitis herpetiformis. Initial dose, 4 Gm.; maintenance dose of 2 to 3 Gm. daily over many months. The disease has responded almost specifically to this drug.

Dosage form. *Tablet*, N. F., 0.5 Gm.

ANTIPROTOZOAN DRUGS

Antiamebic Drugs

While treatment is not entirely satisfactory, clinical management is rather good. Four types of drugs are widely used. Each has some value. Often, it is helpful to utilize two or more types in sequence or "courses" of treatment. One representative of each type has been selected for inclusion. These are: Aureomycin, Carbarsone, Diiodohydroxyquinoline, Chloroquine Phosphate, Emetine Hydro-

effective against cystic and motile (trophozoite) forms in intestinal amebiasis, particularly chronic cases.

Dosage. 2 to 3 Gm. daily until stools remain negative.

Dosage forms. *Capsules* U. S. P., 50 mg., 0.25 Gm.

CARBARSONE, U. S. P. 4-ureidophenylarsenic acid; 28.1% to 28.5% arsenic. White, odorless powder, slightly acid taste. Slightly soluble in water and in alcohol; soluble in solutions of alkali hydroxides and carbonates.

Actions and uses. In intestinal amebiasis, against cystic and motile forms; ineffective in amebic hepatitis. Usually administered orally. Retention enemas may be used in acute amebic dysentery or in resistant cases with motile amebae in the stools. Suitable rest periods required to avoid cumulative arsenic effect.

Toxicity. Occasionally cutaneous disturbances and then toxic reactions of arsenic; rarely, optic nerve injury. Ordinarily not used in presence of hepatitis or kidney damage.

Dosage. Adults. *Oral:* 0.25 Gm. twice daily for 10 days. If necessary, may be repeated after 10-day rest. *Retention enema:* 2 Gm. in 200 cc. warm 2% sodium bicarbonate solution, used after cleansing alkaline enema every other night for maximum of 5 doses; omit oral use.

Children: Dosage reduced according to weight.

Dosage forms. *Capsules* or *tablets* U. S. P., 0.25 Gm.

CHLOROQUINE PHOSPHATE, U. S. P. (For full description see under "Antimalarial Drugs," p. 58.)

Actions and uses. Has been found effective in amebic hepatitis and liver abscess with advantage of extremely lower toxicity than for emetine. Indifferently effective against intestinal amebiasis, therefore used in conjunction with more effective intestinal amebicides.

Dosage. 0.5 Gm. to 1 Gm. daily. Courses vary from 14 to 20 days. Maintenance dose, as needed, approximately 0.5 Gm. biweekly.

Dosage forms. *Tablets,* U. S. P., 0.25 Gm.

DIIODOHYDROXYQUINOLINE, U. S. P.* Colorless or light yellowish powder. Odorless or faint odor; stable in air. It melts with decomposition. Insoluble in water; sparingly soluble in alcohol, and in ether.

Actions and uses. In intestinal amebiasis.

Dosage. Adults: 1 tablet 3 times daily, between meals, for 20 days. Children: 0.2 Gm. per 7 Kg. body weight per day for 20 days, divided into three doses per day.

Dosage form: *Tablets,* U. S. P., 0.65 Gm.

EMETINE HYDROCHLORIDE, U. S. P. Alkaloid of ipecac, or synthetically by methylation of the alkaloid cephaeline. White, slightly yellowish, odorless powder; freely soluble in water or alcohol.

Actions and uses. Especially effective in amebic hepatitis and liver abscess. Does not kill cysts. More effective in early treatment of acute rather than chronic infections. Symptoms relieved within 2 days. Preferably given hypodermically because of emetic effect by mouth.

Toxicity. Practically no margin between therapeutic and toxic doses. Major toxic effect on myocardium. Avoid prolonged administration because of cumulative toxic effects. (Emetine has been found in the urine 2 months after treatment.)

Dosage form. *Injection*, U. S. P., Ampuls, 1 cc., 60 mg. *Tablets*, hypodermic, 30 mg., 60 mg.

Antimalarial Drugs

The search for chemotherapeutic agent(s) which will prevent and cure malaria is still active. To date, however, only p. falciparum malaria can be *cured*. But p. vivax and p. malariae can be *suppressed* more effectively now than heretofore.

For convenient reference, the following is a diagrammatic sketch of the life cycle of the malaria plasmodium in man and mosquito:

Man	Anopheles mosquito
(Asexual, or endogenous cycle; reproduction by schizogony)	(Sexual, or exogenous cycle; reproduction by sporogony)
Stages: trophozoite—schizont—merozoite—trophozoite—etc.	*Stages:* gametocytes (ingested from man)—sporozoite—*to man* trophozoite
gametocytes (sexual form; male and female)	

The following table shows the principal types of malaria and the therapeutic effect of the drugs used. The drugs are described in greater detail, following this table.

Drug	Type of Malaria		
	Benign tertian (*P. vivax*)	Quartan (*P. malariae*)	Malignant subtertian (*P. falciparum*)
Chloroquine [1]	Suppresses asexual forms. Does not kill sporozoites. Gametocidal.	Suppresses asexual forms. Does not kill sporozoites. Gametocidal.	Suppresses asexual forms. Does not kill sporozoites. Partial destruction of gametocytes; impedes formation of *sexual forms*. *Effects complete cure.*
Quinacrine [1]	do.	do.	Do.
Quinine [1]	do.	do.	Do.

[1] More effective than quinine or quinacrine, rapidly terminating acute attacks; also lengthens to a greater extent period between treatment and relapse.

[2] The superiority of chloroquine and of newer agents promises to make quinacrine and quinine obsolete in antimalarial therapy.

CHLOROQUINE PHOSPHATE, U. S. P. (Aralon Diphosphate). 7-chloro-4 (4-diethyl-amino-1-methylbutyl-amino) quinoline diphosphate. White, crystalline, freely water soluble.

Pharmacology. Rapidly and almost completely absorbed from gastrointestinal tract. Deposited in tissues and organs in considerable amounts (liver, spleen, kidneys, lungs; leucocytes hold 200 to 300 times the concentration of drug in the plasma). Chiefly destroyed in the body; 10% to 20% slowly excreted in urine.

Action and uses. See table. Approximately three times as potent as quinacrine; will halt acute attack of falciparum malaria in 1 to 2 days and effect complete cure. Also used in amebiasis (q. v.).

Toxicity. Therapeutic doses may produce slight headache, pruritis, gastrointestinal symptoms, and visual disturbances—seldom serious and apparently

cure most falciparum infections.

Treatment of children:

Age	Initial	In 8 hrs.	On each following 2 days
	Gram	*Gram*	*Gram*
6–18 mo	0. 375	0. 125	0. 25
18 mo.–5 yr	0. 5	0. 25	0. 25
5–8 yr	0. 75	0. 375	0. 375
Over 8 yr	1. 0	0. 5	0. 5

Suppression of vivax. 0.5 Gm. at 7-day intervals. Begin 1 week prior to exposure; also for maintenance after acute attack.

Dosage form. Tablets U. S. P., 0.25 Gm.

QUINACRINE HYDROCHLORIDE, U. S. P. (Atabrine dihydrochloride) 3-Chloro-7-methoxy-9-(1-methyl-4-diethylaminobutyl-amino) acridine dihydrochloride dihydrate. Bitter taste, yellow dye, soluble (1:35) in water, soluble in alcohol.

Pharmacology. Absorbed readily from intestine; excreted slowly in urine and feces.

Action and uses. See table, p. 58. Also useful against giardiasis, and tapeworm (q. v.).

Toxicity and side effect. Dizziness, headache, nausea, emesis, diarrhea. Colors urine yellow; discolors skin, usually disappearing within 2 weeks after therapy is stopped. Gastric irritation allayed by sodium bicarbonate and by taking drug with meals.

Dosage. Treatment of malaria: 0.2 Gm. with 1 Gm. sodium bicarbonate and *glassful of water* every 6 hours for 5 doses; then 0.1 Gm. 3 times daily for 6 days. May be given intramuscularly—0.4 Gm. in 10 to 20 cc. diluent (divide and give in 2 or more sites); then 0.2 Gm. intramuscularly every 8 hours until patient is able to tolerate drug by mouth.

Suppression of malaria (prevents multiplication, not infection!): 0.1 Gm. daily, *with glassful of water*, starting 2 to 4 weeks before exposure, and continuing for at least 4 weeks after last possible exposure in malarious area.

Treatment of *giardiasis:* 0.1 Gm. *with glassful of water* 3 times daily for 5 days.

Dosage form. Tablets, 0.1 Gm.

QUININE SULFATE, U. S. P. White crystalline powder, bitter taste. Soluble 1 in 810 in water; 1 in 120 in alcohol.

Fate. 60% to 90% destroyed in body; remainder chiefly excreted in urine some in feces.

Action and uses. See table, p. 58. Protoplasmic poison. Chief use is antimalarial. Has been used to suppress the myotonus in congenital and atrophic myotonia. May be used (caution!) as a diagnosis test for myasthenia gravis (subclinical symptoms become obvious after quinine). Moderately large doses stimulate uterus.

pregnancy unless absolutely necessary; use cautiously in patients sensitive to drug; contraindicated in optic neuritis; caution in presence of auricular fibrillation.

Dosage. Schedules have varied considerably. The schedule given by the Surgeon General, U. S. Army, in 1943: Treatment: 1 Gm. 3 times daily for 2 days; 0.6 Gm. 3 times daily for 5 days.

Suppression: 0.6 Gm. daily.

In emergency, intravenous use may be employed, using quinine dihydrochloride, 0.65 Gm. diluted in 10 to 20 cc. of isotonic sodium chloride solution. Inject slowly. Avoid extravasation into tissues. Do not repeat more than 3 times in 24 hours. Epinephrine in case of cardiovascular collapse.

Dosage form:

Capsules, U. S. P., 0.3 Gm.

Quinine Dihydrochloride Injection, N. F., *ampuls*, 10 cc. (0.3 Gm.)

Antisyphilitic Drugs

PENICILLIN is superior to and has superseded the arsenic and bismuth compounds.

(See "Antibiotics", chapter 6, for full description and other uses.)

Dosage. *Early and late syphilis:* Dosage schedules vary according to the individual patient. The dosage range is from 600,000 units of penicillin procaine in oil and aluminum monostearate, daily for 3 days, to 600,000 units daily for 10 days. *Minimum dosage*: 600,000 units daily for 3 days.

Central nervous system syphilis: Minimum of 600,000 units daily for 10 days.

Congenital syphilis: 100,000 units per kg. body weight, divided into 10 daily doses. Maximum dosage is that for 60 kg. person (6,000,000 units divided into 10 daily doses), all above 60 kg. receiving the 6,000,000 unit divided dose.

Antitrypanosomic Drugs

Presently accepted therapy includes the use of tryparsamide for late, or CNS, stage of trypanosomiasis and suramin sodium for the early stage.

SURAMIN SODIUM, U. S. P. Hexa-sodium bis-(m-aminobenzoyl-m-amino-gamma-methylbenzoyl-1-naphthylamino-4,6,8-trisulfonate) carbamide. White or slightly pink powder. Odorless, slightly bitter. Very hygroscopic, affected by light. Soluble in water, slightly in alcohol.

Actions and uses. As trypanosomicide, in first stage. Has favorable influence in second stage and has prophylactic effect.

Toxicity. Relatively safe when properly used. Kidney irritant; frequently albuminuria spontaneously disappearing in 6 weeks; sometimes hyaline and granular casts. Great caution in patients with albuminuria. Hemolytic in larger doses. Occasionally dermatitis, chill, fever, nausea, pruritis, headache. Elimination slow; cumulative. Check urine and blood constantly during treatment.

Dosage. Treatment—1 Gm., intravenously, weekly to total of 5 to 10 Gm. Prophylaxis—1 Gm., adult; 0.3 to 0.75 Gm., children; 0.15 to 0.2 Gm., infants. Repeat in 1 week. After 3 months, not before, prophylactic procedure may be repeated.

Dosage form. *Ampul*, U. S. P., 1 Gm.

water (1:2), slightly in alcohol.

Actions and uses. CNS stage of trypanosomiasis.

Toxicity. Worst effect, tendency to produce amblyopia progressing to blindness. Ten to fifty percent of patients develop temporary minor impairment of sion remaining permanent in 5 to 10% of cases and serious permanent damage 1 to 5%. Nitritoid reactions, jaundice, agranulocytosis, hepatitis have been ported. Check eyeground fields before and during administration.

Dosage. Adults, 2 Gm. intravenously, twice weekly for 12 weeks.

Dosage form. *Ampul,* powder, 1 Gm., 2 Gm., 3 Gm.

Chapter 7.

CARDIOVASCULAR DRUGS

Drugs of the digitalis group improve the competence of poorly functioning hearts by directly *increasing* the muscle tone, contractility, responsiveness, and period of refractoriness; by stimulating the vagus center; and by reducing the conductivity of the bundle of His. These actions result in less frequent but stronger heart beats.

In view of the cumulative action of drugs of this group, familiarity with the signs and symptoms of toxicity is very important. Chief among these are digestive symptoms (especially emesis) and arrhythmias. Nausea and vomiting result from direct action on heart, and are roughly proportional to the cardiac therapeutic effect; these symptoms are avoidable only by careful regulation of dose, not by changing mode of administration.

While some differences exist between drugs of this group, they are largely quantitative, depending upon rates of absorption and elimination.

Ordinarily, Powdered Digitalis, U. S. P., is the drug of choice. When there is need for more prompt action, the purified cardiac glycosides have advantage. However, they are more toxic and must be used with caution. The differences between the available preparations are slight, but from the standpoints of speed of action and toxicity, the order of desirability at this time appears to be: Digoxin, U. S. P.; Lanatoside C, U. S. P.; and Digitoxin, U. S. P. Only one such preparation is needed.

DIGITALIS, U. S. P. Dried leaf of *Digitalis purpurea*. Used therapeutically as Powdered Digitalis, U. S. P., 0.1 Gm. of which is equivalent to 1 U. S. P. Digitalis unit (assay conducted on pigeons, using U. S. P. Reference Standard).

Actions and uses. Cardiac tonic; indirectly diuretic. See introductory paragraph for summary of actions. Used in ventricular failure, auricular fibrillation, in conditions such as cardiac enlargement and in mitral stenosis with tachycardia, to prevent circulatory insufficiency.

Toxicity. Poisoning shown by nausea, vomiting, sometimes with abdominal pain, and diarrhea; visual disturbances, various symptoms such as premature contractions, dropped beats, auricular fibrillation, ventricular tachycardia.

Avoid giving calcium together with digitalis as they are synergistic.

Dosage. Intensive method—total of 0.033 Gm. per kg. body weight (*usual* weight, allowing for error in edematous patients). Give one-half the total dose at once; ¼ total dose in 6 hours; smaller fractions every 4 to 6 hours till total dosage or full response is reached.

Intensive method, modified—0.5 Gm. initial; 0.2 Gm. every 6 hours until definite effect (nausea, apex rate, diuresis, or diarrhea).

Effect of intensive methods. Begins in 2 to 4 hours; complete in 12 to 24 hours, persisting after discontinuance, for 4 to 15 days and with partial effect from 1 to 3 weeks after discontinuance.

Effect of cumulative method. Begins in 12 to 24 hours; complete in 24 to 72 hours; persisting after discontinuance, for 4 to 15 days, and with partial effect for 1 to 3 weeks.

Maintenance dose. Usually 0.1 Gm. daily.

Dosage form. *Tablets,* U. S. P., 0.1 Gm.

DIGOXIN, U. S. P. Glycoside from leaves of *Digitalis lanata.* Colorless to white crystals or powder; odorless. Insoluble in water, chloroform, ether. Freely soluble in pyridine and soluble in dilute alcohol.

Action and uses. Similar to digitalis. May be used for rapid digitalization. Effect occurs in a few minutes (ventricular slowing) after intravenous injection, with maximal effect in 1 to 2 hours; after oral dose, effect occurs in a few hours.

Toxicity. As for digitalis.

Dosage. *Caution! It must be established that no drug of the digitalis group has been given the patient for 2 weeks before administering digoxin.*

Rapid digitalization, orally. 0.75 mg. to 1.5 mg. initial, then 0.25 mg. to 0.75 mg. every 6 hours until ventricular rate is between 60 and 70, or maximum therapeutic effect is reached, or toxic symptoms appear.

Very rapid digitalization, intravenously. 0.75 mg. to 1.5 mg. Ventricular slowing usually in a few minutes, and maximal in 1 to 2 hours. If not complete after 6 hours, additional doses of 0.25 mg. to 0.5 mg. may be given i.v. every 6 hours.

Maintenance dose. 0.25 to 0.75 mg. daily, orally, or 0.25 mg. to 0.5 mg. daily i. v.

Note: Digoxin Injection is tissue irritant—dilute contents of ampul with 10 cc. sterile isotonic solution. Inject slowly (5 to 10 minutes); avoid extravenous leakage.

Dosage forms.

Injection, U. S. P. *ampuls,* 1 cc., 0.5 mg.

Tablets, U. S. P. 0.25 mg.

QUINIDINE SULFATE, U. S. P. Dextro-rotatory isomer of quinine. White needle-like crystals, very bitter; soluble in water (1 in 100) and in alcohol (1 in 10).

Actions and uses. Quinidine and quinine are qualitatively similar in action. Quinidine has less antimalarial effect and greater effect on cardiac conduction than does quinine. Quinidine prolongs the refractory period of the heart and reduces its conductivity, and therefore is valuable in combating auricular fibrillation, auricular flutter, paroxysmal tachycardia. There is diminished or little effect in the presence of anatomic lesions and in conditions of long standing.

Toxicity. Similar to quinine sensitivity—nausea, vomiting, convulsions, amblyopia, dyspnoa, asthenia. Quinidine is rapidly excreted, therefore not cumulative.

Dosage. Test dose of 0.2 Gm. (3 gr.) for susceptibility, repeated in 2 hours. If no sensitivity, 0.2 Gm. to 0.4 Gm. three to five times daily, not exceeding 2 Gm. in 24 hours. Maintenance dose, about 0.2 Gm. daily, depending upon extent of control achieved.

Dosage form. *Tablets,* U. S. P., 0.2 Gm. (3 gr.).

Chapter 8.

AGENTS USED IN COUGH THERAPY

The therapeutic management of the cough is directed toward aiding the removal of sputum from the respiratory passages or the depression of cough when it becomes excessive or futile.

The large number of expectorant and cough anodyne agents probably greatly exceeds actual need. The approach here has been to select agents which have had rather general acceptance and which have been effective. Thus, ammonium chloride is selected for general liquefying and expectorant effect; codeine to depress the cough reflex; and potassium iodide for liquefying especially tenacious sputum which has not yielded to other measures, with due regard to its contraindications, as given below. Above all, one should not lose sight of one of the most effective aids to expectoration—water, in liberal amount per os; and as steam inhalation.

AMMONIUM CHLORIDE, U. S. P. Colorless crystals or white powder; cool, saline taste. Soluble 1:2.6 in water; 1:100 alcohol; 1:8 glycerin.

Use. Saline expectorant, for "tight" cough.

Dosage. 0.2 Gm. every 1 or 2 hours or as indicated. May be given in a vehicle of Wild Cherry Syrup, U. S. P. For best effect as a flavor the syrup should be prepared by the U. S. P. method and not by dilution of a concentrate.

Dosage form. Ammonium Chloride Syrup, containing 0.2 Gm. ammonium chloride per 4 cc. of Wild Cherry Syrup, U. S. P.

CODEINE PHOSPHATE, U. S. P. (See "Analgetics", p. 31 for complete description.) By depression of the cough reflex it relieves excessive coughing and the so-called "useless" cough caused by irritation or pressure on the trachea or bronchi. Especially useful at night, to allow undisturbed sleep.

Dosage. 8 mg. every 2 to 3 hours as needed.

Dosage forms. May be given as *tablet* or as "Codeine Phosphate Syrup," containing per 4 cc., Codeine Phosphate, 8 mg. Glycerin, 0.6 cc., Wild Cherry Syrup, U. S. P., q. s. (Glycerin, in addition to some demulcent action, serves to prevent the precipitation of the codeine by the tannic acid present in wild cherry.)

POTASSIUM IODIDE, U. S. P. Crystalline powder; soluble 1:0.7 in water; 1:22 alcohol; 1:2 glycerin.

Use. For excessively thick or tenacious sputum. Produces hyperemia and stimulates secretion of respiratory mucous membrane.

Contraindications. Due to its irritating action, it should not be used during the acute inflammatory stage of bronchitis. Should be avoided in presence of actual or suspected tuberculosis, as it may interfere with connective tissue response.

Dosage. 0.3 Gm. every 2 hours with copious amounts of water.

Dosage forms. Tablets, N. F. 0.3 Gm. May also be given in syrup vehicle, 3 Gm. per 4 cc. of syrup. (Glycyrrhiza Syrup, U. S. P. is a good vehicle.)

Chapter 9.

AGENTS USED IN DENTAL PRACTICE

Drugs used exclusively in dental practice are described in detail. Those used in other fields as well as in dentistry are mentioned by name, and reference should be made to the therapeutic groups in which they are described. The listing here is by therapeutic groups, in alphabetical order.

Analgetics

SALICYLATES: ACETYLSALICYLIC ACID, U. S. P.
OPIUM DERIVATIVES: MORPHINE, AND CODEINE PREPARATIONS.
NONOPIATE, ADDICTING ANALGETICS: MEPERIDINE (DEMEROL).
ACETOPHENETIDIN.

Anesthetics, General

GASES.
VOLATILE LIQUIDS.
SOLIDS (THIOPENTAL SODIUM, U. S. P.)

Anesthetics, Local

ETHYL AMINOBENZOATE, U. S. P.
ETHYL CHLORIDE, U. S. P.
LIDOCAINE HYDROCHLORIDE, N. N. R. (XYLOCAINE)
PROCAINE HYDROCHLORIDE, U. S. P.

TETRACAINE HYDROCHLORIDE, U. S. P. (PONTOCAINE). For local injection a 0.15 percent solution is added to a 2 percent solution of procaine with epinephrine 1:100,000.

Anti-infectives, Local

ALCOHOL.
ANTIBIOTICS (PREPARATIONS FOR LOCAL USE)
BENZALKONIUM CHLORIDE, U. S. P.
SAPONATED CRESOL SOLUTION, U. S. P.

CRESOLATED FORMALDEHYDE, N. F. V. Consists of orthocresol (40 percent) and formaldehyde solution (60 percent). Used for the disinfection of putrescent pulp canals during the first phase of root canal therapy. *Caution* must be observed in applying this material to prevent necrosis of the periapical tissues. ***Dosage:*** All necrotic pulp tissue is removed by instrumentation and a cotton point moistened with the solution is placed in the canal. The point should not extend beyond the apex of the root.

FORMALDEHYDE SOLUTION, U. S. P.

HYDROGEN PEROXIDE SOLUTION, U. S. P. (3% hydrogen peroxide). A colorless liquid with an ozone-like odor. Acts as germicide by reason of its

oxygen gas upon contact with tissues, hydrogen peroxide should not be used to irrigate wounds of deep cavitation or sealed into a root canal; the patient may experience severe pain and infection may be forced into the surrounding tissues. *Dosage:* The solution is diluted with equal parts of water and the area to be treated is sprayed with the atomizer with as much air pressure as can be used without causing pain. An irrigating syringe may be used in isolated areas if there is proper access.

IODINE TINCTURE, U. S. P.

PHENOL, U. S. P. Colorless crystals; soluble in water (1:15). Antiseptic and germicide. Used to disinfect cavity preparations prior to the insertion of a restoration. *Dosage:* The preparation used is Liquefied Phenol, U. S. P. (approx. 88% phenol; rest, water). Area to be treated is cleaned, isolated with cotton, and the phenol applied on a pledget of cotton. The phenol may then be removed with a pledget of cotton moistened with alcohol. Care should be taken to avoid contacting the soft tissues with this escharotic.

AMMONIACAL SILVER NITRATE SOLUTION, N. F. Contains approximately 30 percent of readily reducible silver. It is claimed that this preparation is less toxic than silver nitrate per se. Used in dental practice as germicide for cavity preparations. Its use is based on its ready diffusibility into the dentin. It is thought that the finely divided silver that is deposited in the dentinal tubules may retard the progress of caries in dentin. Because of its staining properties its use is confined to the posterior teeth. It is also used to desensitize hypersensitive dentin and cementum. *Dosage:* Applied to the area to be treated on a small wisp of cotton or special applicator; solution is reduced with eugenol, 10 percent formaldehyde, or hydroquinone.

Anti-infectives, Systemic

ANTIBIOTICS.
SULFONAMIDES.

Hemostatic Agents

ABSORBABLE GELATIN SPONGE.
VITAMIN K.
TANNIC ACID, N. F.
EPINEPHRINE SOLUTION, U. S. P.

Respiratory Stimulants

DIRECT STIMULANTS.
REFLEX STIMULANTS.

Sedatives and Hypnotics

ALDEHYDE DERIVATIVES.
BARBITURIC ACID DERIVATIVES.

Spasmolytics

AMYL NITRITE, U. S. P.
ATROPINE SULFATE, U. S. P.
SCOPOLAMINE HYDROBROMIDE, U. S. P.

PHENYLEPHRINE HYDROCHLORIDE, U. S. P. (NEO-SYNEPHRINE).

NORDEFRIN HYDROCHLORIDE, A. D. R. (COBEFRIN). Qualitatively similar to epinephrine in action. Said to cause less central nervous system-disturbance following injection. Used as a vasoconstrictor in combination with procaine and other local anesthetics in concentration 1:10,000. May be applied as homostatic to bleeding mucous membrane, in 1:200 solution.

Vitamins

As in "Vitamins," ch. 27.

Miscellaneous Drugs

These agents are listed according to the special phase of practice in which they are employed.

Operative

SODIUM FLUORIDE. White odorless powder; one part soluble in 25 parts water. Solutions of sodium fluoride applied to the teeth of children apparently limit the amount of tooth decay that may occur to the permanent dentition if the permanent teeth are not carious at the time they are treated. The mechanism of action is not understood at present. *Dosage:* A 2 percent aqueous solution is employed. The teeth to be treated are cleansed (prophylaxis), isolated with cotton rolls, dried with compressed air, and the crowns wet with the solution. The solution is permitted to dry on the teeth for 3 to 5 minutes, the rolls removed, and the patient dismissed. Four such treatments are given 1 week apart. At present it is thought that the series should be given at 3, 7, 10, and 13 years of age.

SODIUM FLUORIDE PASTE. Consists of equal parts of sodium fluoride, kaolin, and glycerin. Used to desensitize hypersensitive dentin and cementum. *Dosage:* Isolate area to be treated and dry; apply paste to cover area, and allow to remain in contact for 3 minutes. *Avoid contact of paste with soft tissue.*

ZINC OXIDE, U. S. P. White odorless powder; insoluble in water and alcohol. Used with eugenol to form a protective sedative cement. May be employed in this manner to relieve odontalgia associated with pulp hyperemia and pulpitis; and as a sedative protective following gingivectomy.

EUGENOL, U. S. P. Colorless or pale yellow liquid with pungent odor and taste. Used to reduce silver nitrate in cavity "sterilization." Employed as a protective and anodyne over exposed pulps. (See Zinc Oxide, above.)

Periodontia

ZINC CHLORIDE, N. F. White granular powder; used as an astringent in the treatment of periodontal pockets. *Dosage:* 8 percent solution is used. Pledget of cotton is moistened with the solution and placed in the pocket to be treated. The area should be cleaned and isolated with cotton rolls before the solution is applied and care should be taken to confine the material to the area being treated.

TRICHLOROACETIC ACID, U. S. P. Colorless deliquescent crystals. A caustic used for the removal of hyperplastic gingival or pulp tissue, and for the symptomatic treatment of aphthous ulcers. *Caution* should be exercised in the use of this material due to its highly corrosive action.

appliances. Also used to seal local anti-infectives and sedative agents in gingival pockets.

Endodontia

HYDROGEN PEROXIDE, 30 PERCENT. Employed as a bleaching agent to remove the stain from nonvital teeth and the stains from mottled enamel. *Dosage:* 5 cc. of 30 percent solution is mixed with 1 cc. of ether; the two liquids are not miscible and should be stirred immediately before application. Care should be taken to protect the soft tissues. The details of the technique should be reviewed before using this material.

Mouth Wash

A solution of 2% sodium bicarbonate and 1% sodium chloride in water is an effective cleanser.

Chapter 10.

AGENTS USED IN DERMATOLOGIC PRACTICE

Dermatologic therapy employs both internal and external measures but is dependent for the greater part upon local treatment. A wide range of therapeutic agents has become associated with cutaneous therapy probably in part because the pathogenesis and etiology of many skin diseases are little understood and also because the pharmacology of several useful dermatologic preparations is yet to be fully determined. Nonetheless, there is no branch of medicine with so many possible remedies as in dermatologic therapy.

The choice of medicament and the form of treatment for a cutaneous disease may vary with the experience and the art of the therapist, and in many instances the therapy is employed on a purely empiric basis. In general, however, the vehicles and the incorporated agents are selected on the basis of the morphologic characteristics (acute, subacute, or chronic), the localization, and the diagnosis of the eruption. The use of the selected drug and its vehicle is directed toward attaining certain pharmacologic effects upon the disease process by way of the inherent physical and chemical properties of the medication.

Individual response to drugs cannot always be predicted but better therapeutic results can be expected by properly employing those drugs whose pharmacologic effects are reasonably well established.

The following may be used as a basic grouping of pharmacologic effects, and of the vehicles (carriers) and incorporated active agents used in topical therapy to obtain these effects.

PHARMACOLOGIC EFFECTS

Anti-infective (antibacterial, antifungus, antiparasitic).

Destruction or the inhibition of growth of bacteria, fungi, or parasites on the skin.

Antibacterial

Antibiotics:

Aureomycin, U. S. P.

Bacitracin, N. N. R.

Tyrothricin Solution, U. S. P.

Mercurials:

Ammoniated Mercury, U. S. P. (1–10%)

Mercury Bichloride, U. S. P. (1:1,000)

Other:

Hydrogen Peroxide Solution, U. S. P.

Iodochlorhydroxyquin, U. S. P. (Vioform)

Methylrosaniline Chloride, F.

Iodine, U. S. P.
Methylrosaniline Chloride, N. F.
Potassium Permanganate, U. S. P.
Salicylic Acid, U. S. P.
Sodium Thiosulfate, N. F.
Undecylenic Acid, N. F., and its salts:
Copper Undecylenate.
Zinc Undecylenate, N. F.

Antiparasitic
Benzene Hexachloride, N. N. R.
Precipitated Sulfur, U. S. P.

Antiphlogistic.

Reduction of an inflammatory process by cooling, vasoconstriction, o astringency.

Aluminum Acetate Solution, U. S. P. (or comparable solution).
Boric Acid, U. S. P. (1-2% solution).
Potassium Permanganate, U. S. P. (1:4,000-1:10,000, fresh solution).
Sodium Chloride Solution, isotonic, U. S. P.
Soothing baths: Starch; Oatmeal ("Aveeno").

Antipruritic and analgetic:

Relief of itching and pain.

Local:
Camphor, U. S. P. (⅛-5%)
Chloral Hydrate, U. S. P. (1-5%)
Menthol, U. S. P. (⅛-½%)
Phenol, U. S. P. (½-1%)
Sodium Thiosulfate, N. F. (25%)

Oral:
Histamine-antagonizing agents:
Diphenhydramine, U. S. P. (Benadryl)
Thonzylamine, N. N. R. (Neohetramine)
Tripelennamine, U. S. P. (Pyribenzamine)

Astringent, caustic:

Aluminum Chloride, N. F.
Cupric Sulfate, U. S. P.
Zinc Sulfate, U. S. P.

Detergent.

Substitute for soap to avoid irritation. See text, p. 79, under "So Substitutes."

Emollient.

Softening of the skin. Fatty ointments and oils of animal, mineral, or ve table origin.

Animal:
Cholesterol, U. S. P.
Wool Fat, U. S. P.
Hydrous Wool Fat, U. S. P.

Petrolatum, U. S. P.; White Petrolatum, U. S. P.
Liquid Petrolatum, U. S. P.

Vegetable:

Linseed Oil, U. S. P.
Olive Oil, U. S. P.
Peanut Oil, U. S. P.

Keratolytic.

Reduction or removal of the keratin (horny) layer of the skin.

Anthralin, N. F. ($^1/_{10}$–1%)
Betonaphthol, N. F. (5%)
Podophyllum Resin, N. F.
Resorcinol, U. S. P. (2–30%)
Salicylic Acid, U. S. P. (greater than 5%)
Silver Nitrate (5%, 10%)
Toughened Silver Nitrate, N. F. (Silver Nitrate Pencils)
Precipitated Sulfur, U. S. P. (greater than 5%)
Trichloroacetic Acid, U. S. P. (full strength)

Keratoplastic.

Establishing a more normal keratinization and thickening of the layer.

Salicylic Acid, U. S. P. (less than 5%)
Precipitated Sulfur, U. S. P. (less than 5%)
Tars (up to 5%). (See "Tars and Tar Derivatives", p. 79.)

Protective.

Physical and chemical properties of protecting the skin against mech chemical, and physical agents.

Lotions, ointments, pastes containing the following as may be indicate

Calamine, U. S. P.
Starch, U. S. P.
Sunscreen agents:
Absorptive agent: Isobutyl-paro-aminobenzoate (Cyclolorm)
Blocking agent: Titanium Dioxide, N. F.
Talc, U. S. P.
Zinc Oxide, U. S. P.

Flexible Collodion, U. S. P.

AGENTS USED

The preceding pharmacologic effects are accomplished by the use of agents and of vehicles (carriers). Most vehicles occur as solutions, p lotions, liniments, ointments, pastes, tinctures, or plasters.

The following listed remedies represent those which have been foun useful for the management of the more common dermatologic conditi countered. The remedies are classified under two general headings:

I. Topical Agents (grouped according to physical characteristics, e. g tions, lotions, powders, pastes, etc.); and

II. Systemic Agents (grouped according to mode of administration, ' parenteral)

Solutions for General Use	
Baths:	50 gal. is approximate volume for adult bath
Colloid:	
Starch and sodium bicarbonate:	Make paste with cold water and add to tub of warm water
Starch, 1 cup	
Sodium bicarbonate, 1 cup.	
Oatmeal	"Aveeno" is a type suitable for this purpose.
Medicated:	
Potassium Permanganate:	
1:10,000, 1:32,000	
Sulfur Bath:	
Sulfurated Lime Solution, N. F.	"Vleminckx' Solution" 90 cc. (3 oz.) to 50 gal. water.
Tar Bath	
Coal Tar Solution, N. F.	"Liquor Carbonis Detergens"
Coal tar, 20% in alcohol, dispersed with quillaja.	90 cc. (3 oz.) to 50 gal. water.

Wet Dressings. For acute inflammatory processes where weeping and crusting is present. Also effective in cleansing the skin of debris, relieving edema, and pruritus.

Dressings may be used either hot or cold. Open dressings allow evaporation and therefore they are preferred over closed impermeable dressings. No more than one-third of the body surface should be dressed at one time.

Soaking of the affected part in the solution for short periods of time will accomplish much the same effect as the wet dressing.

Aluminum Acetate	*Use:* Effective astringent which reduces inflammation and facilitates drying in the acute weeping eruptions.
Aluminum Acetate Solution, U. S. P.	"Burow's Solution"
5% aluminum acetate, pH of approximately 4.	Dilute 1:10–1:20 for use.
Aluminum Acetate Solution Powder:	
Aluminum sulfate and calcium acetate yielding a solution of same pH as the U. S. P. solution.	1 level teaspoonful stirred in 1 quart of water makes a solution of 1:20 with pH of approximately 4.
Potassium Permanganate	*Use:* Treatment of acute inflammatory processes. Particularly effective for weeping eruptions with secondary infection. It is deodorant, disinfectant, astringent. (Stains tissue and linen.)

Sodium Chloride

Use: In isotonic and slightly hyp
tonic solution, effective in rednes
inflammation and weeping.
2 teaspoonfuls in 1 quart of water (
Gm. per quart) makes appro
mately isotonic solution.

Solutions for Specific Use

Acetic Acid, ½-1% concentration

Aluminum Chloride Solution

Aluminum Chloride, N. F.,	25%
Alcohol,	
Water, equal parts of each to make	100%

Chloroformic Anthralin Solution

Anthralin, N. F.,	5%
Chloroform, to make	100%

Petroleum Benzin, U. S. P.

Boric Acid Solution — 1 teaspoonful to glass of water.

Coal Tar Solution, N. F. — "Liquor Carbonis Detergens"

Coal Tar	20%
Quillaja	10%
Alcohol, to make	100%

Use: Keratoplastic, antipruritic. Eff
tive in the chronic and subac
dermatoses. (It is a photosen
tizing agent.) May be added
lotions, ointments, pastes; finish
product to contain 2 to 8% of t
solution.

Chloroformic Coal Tar Solution, N. F.

Coal Tar,	5%
Chloroform, to make	100%

Flexible Collodion, U. S. P.

Copper and Zinc Sulfates Solution — "Dalibour's Solution"

Cupric Sulfate,	10. 0
Zinc Sulfate,	14. 0
Water, to	500. 0

Copper Undecylenate Solution

Copper Undecylenate,	10%
Undecylenic Acid,	5%
Tetrachloroethylene,	
Isopropyl Alcohol,	
Dioctyl Sodium Sulfosuccinate, N. F., equal parts of each to make	100%

Hydrogen Peroxide Solution, U. S. P.

3% Hydrogen Peroxide

Iodine Tincture, U. S. P.

Podophyllum Resin, Alcoholic		"Podophyllin, Alcoholic"
Podophyllum Resin, N. F.,	20%	
Alcohol, to make	100%	
Podophyllum Resin, Oily		"Podophyllin, Oily"
Podophyllum Resin, N. F.,	25%	
Liquid Petrolatum, to make	100%	
Salicylic Collodion, N. F.		
Salicylic Acid,	10%	
Flexible Collodion, to make	100%	
Silver Nitrate Solution		5% and 10% solutions
Sodium Thiosulfate Solution		25% solution
Sulfurated Lime Solution, N. F.		"Vleminckx' Solution"
Active ingredients: Calcium trisulfide, calcium thiosulfate		
Tar Collodion		
Coal Tar,	70%	
Acetone,	15%	
Flexible Collodion,	15%	
Tyrothricin Solution, U. S. P.		2% and 2.5%, diluted before use

Powders

Powders are used as (1) drying agents because of their moisture-absorbing properties; (2) astringents; (3) antipruritic agents; (4) fungistatic agents.

Sodium Bicarbonate and Talc Powder		*Use:* Deodorant.
Sodium Bicarbonate,	10%	
Talc, to make	100%	
Talc, U. S. P.		*Use:* Useful in nonweeping intertriginous areas.
Compound Undecylenic Acid Powder		*Use:* Locally, to dry superficial fungus infections; used as preventive agent.
Zinc Undecylenate, N. F.,	20%	
Undecylenic Acid, N. F.,	2%	
Talc, U. S. P.	78%	

Lotions and Liniments

Lotions and liniments are convenient vehicles for covering wider areas of the body surface. Lotions are intended as drying agents and may carry antipruritic agents, desquamating agents, and stimulating agents. They are good vehicles for carrying desquamating agents to the scaly scalp. Liniments serve the same purpose as lotions but are composed of a high proportion of oil which tends to be less drying to the skin.

Lotions

Calamine Lotion, U. S. P.		
Calamine,	8%	May add:
Zinc Oxide,	8%	Menthol, ¼%
Polyethylene Glycol 400,	8%	Phenol, 1%
Polyethylene Glycol 400 Monostearate,	2%	(If phenol, 1%, is added, double the amount of polyethylene glycol 400
Water, to make	100%	

Chloral Hydrate,	2.0	caused by resorcinol.
Salicylic Acid,	2.0	
Mercury Bichloride,	0.1	
Glycerin,	2.0	
Diluted Alcohol, U. S. P., to	120.0	
Chloral Hydrate Scalp Lotion, Oily		For *light hair, with excessively dry scalp.* Additional castor oil may be added as indicated.
Chloral Hydrate,	2.0	
Salicylic Acid,	2.0	
Mercury Bichloride,	0.1	
Castor Oil,	2.0	
Alcohol, 70%, to	120.0	
Resorcinol Scalp Lotion		For *dark hair.*
Resorcinol,	2.0	
Salicylic Acid,	2.0	
Mercury Bichloride	0.1	
Glycerin	2.0	
Diluted Alcohol, U. S. P., to	120.0	
Resorcinol Scalp Lotion, Oily		For *dark hair, with excessively dry scalp.* Additional castor oil may be added as indicated.
Resorcinol,	2.0	
Salicylic Acid,	2.0	
Mercury Bichloride	0.1	
Castor Oil	2.0	
Alcohol, 70%, to	120.0	
Tar Scalp Lotion		
Coal Tar Solution, N. F.	8.0	
Salicylic Acid	2.0	
Camphor Water, U. S. P.	45.0	
Alcohol	95.0	
Water, to make	180.0	
Sunlight Protective:		
Cycloform Lotion		*Use:* Chemical absorptive solution as protective in cases of sunlight sensitivity; lupus erythematosus.
Isobutyl-para-aminobenzoate (Cycloform)	5%	
Glycerin	5%	
Alcohol, to make	100%	
White Lotion, N. F.		"Lotio Alba"
Zinc Sulfate,	4%	Solution must be freshly prepared.
Sulfurated Potash,	4%	Dispense maximum of 90 cc. (3 oz.). Portions in excess of 90 cc. usually will have deteriorated before being used.
Distilled Water, to make	100%	*Use:* Mild peeling, stimulating, drying, antiseborrhoic action. Especially useful in treatment of acne vulgaris and acne rosacea.

Water	40.0

Camphor	1%
Coal Tar Sol.,	5% of sol.
Resorcinol,	1%, 4%
Salicylic Acid,	1%
Precipitated Sulfur	6%
Neutracolor (for flesh tint)	2%

Zinc Oxide Oil Lotion

Zinc Oxide,	20.0
Talc,	20.0
Olive Oil,	10.0
Calcium Hydroxide Solution, to make	120.0

Use: For moist effect.

May add:

Chloral hydrate	5%
Coal Tar Sol.,	5% of sol.
Ichthammol,	5%
Phenol,	½%
Resorcinol,	1%, 4%
Neutracolor,	2%

Liniments

Liniments are emulsions of oil and water. They are useful in that they can carry most active agents, are less drying than lotions and almost as penetrating as ointments. Can be used over large areas for soothing, antipruritic, stimulative effects in the subacute and chronic dermatoses.

Calamine Liniment, N. F.

Calamine,	8%
Zinc Oxide,	8%
Olive Oil,	50%
Calcium Hydroxide Solution, to make	100%

May add:

Coal Tar Sol.,	5% of sol.
Menthol,	¼%
Phenol,	½%

Ointments and Pastes

Ointments and pastes are used as vehicles which stay in place, offer protection, or, in some instances, afford penetration of the active ingredients. Ointments are not the medication of choice on acute oozing and infected surfaces where the necessity of drainage is important. Water washable bases are now available as vehicles for most of the active agents and are especially suitable for use on the hairy areas.

Ointments

Anthralin Ointment, N. F.	*Use:* For extremely chronic indolent lesions.
Anthralin, 0.1%, 0.25%, 0.5%, or 1%	
White Petrolatum, to 100%	
Aureomycin Ointment	*Use:* For aureomycin-sensitive organisms.
Aureomycin, 3%	
White Petrolatum, to 100%	
Bacitracin Cream	*Use:* Antibacterial cream of low sensitizing index.
Bacitracin, 500 units per gram	
Water, 1%	*Storage:* In refrigerator. Discard after 30 days.
Hydrophilic Ointment, to 100%	

1%, in a washable base.

Betanaphthol-Sulfur Ointment

Betanaphthol,	2.0
Precipitated Sulfur,	4.0
Peruvian Balsam,	15.0
Petrolatum,	15.0

Benzoic and Salicylic Acid Ointment, N. F.

Benzoic Acid,	12%
Salicylic Acid,	6%
Wool Fat	
White Petrolatum, of each, to	100%

Coal Tar Ointment, U. S. P.

Coal Tar,	5%
Zinc Oxide Paste, to	100%

Hydrophilic Ointment, U. S. P.

Stearyl Alcohol,	25.0
White Petrolatum,	25.0
Glycerin,	12.0
Sodium Lauryl Sulfate,	1.0
Methylparaben,	0.025
Propylparaben,	0.015
Distilled Water,	37.0

Ichthammol-Zinc Oxide Ointment

Ichthammol,	3%
Zinc Oxide Ointment, to	100%

Iodochlorhydroxyquin Cream

Iodochlorhydroxyquin, U. S. P. (Vioform) in suitable washable base 3%

Juniper Tar Ointment

Juniper Tar,	1 to 5%
Zinc Oxide Ointment, to	100%

of surrounding normal skin to insure adequate treatment. Patient should not wash hands or hair for 24 hours. When applied to the scalp, towel should be worn over the head for one hour after application. If first application unsuccessful, second may be made after one week.

Linen and pillow cases should be boiled; woolen clothes dry-cleaned.

Use: Strong peeling ointment. In severe acne rosacea with rhinophyma.

Rub into affected areas only; keep away from eyes. Apply 3 times daily for 3 days and then apply mild ointment.

"Whitfield's Ointment"

Use: Keratolytic, macerating; effective fungicide on nonexudative area.

May be diluted to one-half or one-fourth strength.

Use: See "Tar and Tar Derivatives", p. 79.

May add:

Salicylic Acid, 1 to 5%

"Emulsion Base"

Use: Washable base readily removed from skin and clothing, with water.

Effective carrier (where preferred to the official base) for:

Ammoniated Mercury,	2%
Salicylic Acid,	1–5%
Precipitated Sulfur,	1–5%

Tars

Use: See "Tars and Tar Derivatives", p. 79.

"Vioform Cream"

Use: Antibacterial.

Use: See "Tars and Tar Derivatives", p. 79.

May add:

Salicylic Acid 1–5%

White Ointment, U. S. P., to 100%

Pine Tar Ointment
Pine Tar 1 to 5%
Zinc Oxide Ointment, to 100%

Rose Water Ointment, U. S. P.
A blend of spermaceti, white wax, expressed almond, or persic oil, sodium borate, rose water, rose oil, water.

Sulfur Ointment, U. S. P.
Precipitated Sulfur, 10%
Liquid Petrolatum, 10%
White Ointment, U. S. P., to 100%

Compound Undecylenic Acid Ointment, N. F.
Undecylenic Acid, 5%
Zinc Undecylenate, 20%
Polyethylene glycol ointment, to 100%

White Petrolatum, U. S. P.

Zinc Oxide Ointment, U. S. P.
Zinc Oxide, 20%
Liquid Petrolatum, 15%
White Ointment, U. S. P., to 100%

Pastes

Aluminum Acetate Paste
Aluminum Acetate Sol., U. S. P., 10.0
Wool Fat 20.0
Zinc Oxide Paste, 30.0

Zinc Gelatin, U. S. P.
Zinc Oxide, 10%
Gelatin, 15%
Glycerin, 40%
Distilled Water, to 100%

Zinc Oxide Paste, U. S. P.
Zinc Oxide, 25%
Starch, 25%
White Petrolatum, to 100%

Use: See "Tars and Tar Derivatives", p. 79.
May add:
Salicylic Acid, 1–5%
Use: Emollient; may also be used as base for other agents (sulfur, coal tar, etc.)

Use: Antiseborrheic agent. May be dispensed in ½ or ¼ strength, diluted with White Ointment, U. S. P.
May add:
Salicylic Acid, 1–5%
Use: Mild fungicidal agent for subacute and chronic infections.

Use: Water repellent, greasy, protective emollient. May be used alone or as vehicle for most active ingredients.
Use: Vehicle; protective.

Use: Soothing, softening, protective paste. May be used intermittently with wet dressing treatment in order to avoid excessive maceration.
Pastes should be removed with liquid petrolatum or vegetable oils rather than scrubbed free of the surface.
"Zinc Gelatin Boot", "Unna's Zinc Gelatin Boot"

"Lassar's Plain Zinc Paste"
Use: Protective; drying.
May add:
Coal Tar (See Coal Tar Ointment, USP, which contains 5% Coal Tar in Zinc Oxide Paste.)

Salicylic Acid in suitable plaster base.

Note. 40% plaster is used, for keratolytic effect.

Soap Substitutes

Soap substitutes are used in many instances of inflammatory dermatoses where it is desirable (1) to reduce or avoid contact with the usual alkali content of soap, or (2) to control exposure of the patient to contactants by eliminating soaps and cleansers of unknown composition and irritant potential.

Preparations. Various preparations are available consisting of sulfonated oils and sulfonated creams.

Tar and Tar Derivatives

The tar derivatives are among the most useful therapeutic agents in dermatologic therapy. Their exact mode of action is unknown but their effect on psoriasis and other diseases exhibiting parakeratosis suggests that they influence the conversion of the S–H bonds to an S–S linkage restoring the normal keratinization cycle. A basic list of tar compounds is difficult to enumerate because there is great individual variation in tolerance. A few of the more commonly used preparations are therefore presented in the order of their pharmacologic potency:

ICHTHAMOL (Ammonium ichthosulfonate). Included with tars because of keratoplastic action. *It is mild and may be used in subacute dermatoses.* Usually, 3% in Zinc Oxide Ointment. (See Ichthammol-Zinc Oxide Ointment, under "Ointments.")

WOOD TARS (Pine Tar; Juniper Tar). These tars are stronger than ichthammol and usually are used 1–5% with salicylic acid. (See Pine Tar Ointment, and Juniper Tar Ointment, under "Ointments.")

COAL TAR. This is the most healing and also the most irritating of the tar compounds. For use in subacute and chronic dermatoses.

COAL TAR SOLUTION, N. F., 1–10% of the Solution, in ointments and in lotions.

CHLOROFORMIC COAL TAR SOLUTION, N. F.

COAL TAR, 1%, 3%, 5%, 10% in various ointments. (See Coal Tar Ointment, U. S. P., under "Ointments.")

2. SYSTEMIC AGENTS

Oral

BISMUTH SODIUM TRIGLYCOLLAMATE, N. N. R. (Bistrimate). Each tablet contains 0.41 Gm. equivalent to 75 mg. of elemental bismuth.

Use. May be used for the treatment of chronic lupus erythematosus and lichen planus. (Toxic effects may be noted, e. g., generalized pruritus, toxic erythemas, "bismuth line," gastrointestinal upsets, stomatitis, peripheral neuritis, myalgias, transient leukopenia.)

Dosage. 1 tablet 3 times daily for 3 days; thereafter, 2 tablets daily. May be continued for 26 weeks unless contraindications ensue.

barbiturates which may be sensitizing to the skin. Paraldehyde is the drug of choice for this purpose. However, it would not be acceptable to some patients for this purpose, because of its taste and clinging odor. Choral hydrate is therefore included in this chapter only, since, with the exception of paraldehyde, it is least sensitizing to the skin.

Dosage. 1 Gm. before retiring. Give well diluted in fruit juice, to disguise flavor.

Dosage form. Chloral Hydrate *Syrup* (Chloral Hydrate, 1 Gm. in Syrup, U. S. P., to make 4 cc.). Other vehicles may be used as desired. Probably the best flavor disguise is accomplished by diluting the dose in fruit juice.

HISTAMINE-ANTAGONIZING AGENTS. See chapter 15 (Histamine-Antagonizing Agents).

POTASSIUM ARSENITE SOLUTION, N. F. (Fowler's Solution).

Use. May be used in chronic cases of lichen planus, dermatitis herpetiformis, pemphigus, psoriasis. The indications for use will depend upon the experience of the therapist. (Toxic effects may ensue, e. g., abdominal discomfort, colic, diarrhea, swelling of the face and eyelids, erythema, thready pulse. The drug is known to produce arsenical keratoses when used for long periods of time.)

Dosage. Increasing dosage beginning at 0.1 cc. and advancing to 0.3 cc. three times daily. Rest periods are advocated.

OTHER SYSTEMIC AGENTS such as antibiotics, hematics, hormones, sedatives, sulfonamides, vitamins, laxatives, are prescribed as indicated.

Parenteral

ANTIBIOTICS. See p. 53.

BISMUTH SUBSALICYLATE INJECTION, U. S. P.

Use. Treatment of lichen planus, lupus erythematosus, extensive verrucae.

Dosage. 1 cc. (0.13 Gm.) deep intramuse. Injection weekly for 8 to 12 weeks, followed by a rest period. (Toxic effects: Bismuth line on gums, stomatitis, albuminuria, various dermatoses, jaundice.)

CALCIUM GLUCONATE. (See chapter 17, p. 109, on "Agents used in Metabolic Disorders.")

COCCIDIOIDIN. 1:100 extract for intradermal skin test for coccidiomycosis. Usual dose: 0.1 cc. Available in 1 cc. (10 tests) vial.

DIMERCAPROL INJECTION, U. S. P. (BAL).

Use. To combat arsenic, mercury, chrome, and gold intoxication.

Toxicity. Dimercaprol is contraindicated in hypertension and in cardiac disease. The drug must be used with extreme caution for it is capable of causing toxic and systemic poisoning effects of its own.

Dosage form. BAL in Oil *Ampuls*, 10%, 4.5 cc.

DUCREY SKIN TEST. (Diagnostic material for chancroid (soft chancre); see chapter 11, p. 82, on "Diagnostic Aids."

EPINEPHRINE. See chapter 26, p. 137, "Sympathomimetic Amines."

FREI TEST ANTIGEN. (Diagnostic antigen for skin testing in lymphogranuloma venereum; see chapter 11, p. 83, on "Diagnostic Aids.")

PROCAINE. See chapter 4, page 39, "Local Anesthetics."

TRYCHOPHYTON: For diagnostic test for trichophytosis. Prepared from Trichophyton interdigitale. Available in 5 cc. vial.

VITAMIN A.

Use. Useful in treatment of comedone acne, follicular hyperkeratoses, keratosis follicularis, pityriasis rubra pilaris.

Dosage. 50,000–200,000 units daily, intramuscularly.

Dosage forms. *Ampuls*, 1 cc. containing 20,000 units, 50,000 units, 100,000 units.

VITAMIN B COMPLEX INJECTABLE. See chapter 27, p. 143, "Vitamins."

Chapter 11.

DIAGNOSTIC AIDS

This section deals with agents used for various diagnostic purposes. Although numerous agents are in use for the various tests, the selection here has been limited to those in standard use.

CHANCROID

DUCREY VACCINE. Saline suspension of killed Ducrey's bacilli.
Dosage. 0.1 cc. intracutaneously. Test is read in 48 to 72 hours.
Dosage form. *Vials*, 0.2 cc. (2 tests); 5 cc. (50 tests).

CIRCULATION TIME

Circulation time is the measured interval from the time of injection of a drug traveling the shortest path through the circulatory system to reach a designated site where it produces a characteristic physiologic or physical response.

Many drugs have been used such as histamine (facial flush), sodium cyanide (sudden deepening of respiration), fluorescein, ultraviolet radiation, papaverine hydrochloride, etc. Recently, subjective methods have come into wider use, such as calcium chloride, magnesium sulfate, calcium gluconate, etc.

ETHER. 0.3 cc. ether is added to 0.6 cc. sterile isotonic sodium chloride solution. Injected into antecubital vein, using an 18-gauge needle. *Circulation* through the right side of the heart is checked by determining time taken by drug to travel from antecubital vein to the lungs. *End Point:* Facial grimace, cough, or perception of the ether by the subject or the observer. If there is a septal (atrial or ventricular) defect a transient facial paresthesia may occur. Normal "arm to lung" time: 3 to 8 seconds.

SODIUM DEHYDROCHOLATE INJECTION, N. F. (20%). To check circulation through left side of heart. End point involves peripheral circulation. "Arm to tongue" time is determined. Inject 5 cc. of solution rapidly into antecubital vein. Bitter taste is produced, passing rapidly from base to tip of the tongue and rapidly diminishes. Normal "arm to tongue" circulation time is 9 to 16 seconds.

Dosage form. Sodium Dehydrocholate *ampuls*, 20% in various sizes.

KIDNEY FUNCTION

PHENOLSULFONPHTHALEIN, U. S. P. Readily absorbed from the tissues and excreted mainly in the urine. Injected intravenously, excretion begins in 5 to 10 minutes in normal patients; 25–45% normally excreted in 15 minutes, and 50–60% in the first hour; 65–85% at end of second hour.

Dosage. 1 cc. of 0.6% solution.

Dosage or 1 cc. *ampuls* (0.6% [illegible] 6 mg.)

SULFOBROMOPHTHALEIN SODIUM, U. S. P. (Bromsulphalein). This dye normally is rapidly removed from blood stream by the liver (and excreted in the bile).

Dosage. Intravenous injection of 5 mg. per kg. body weight normally is completely removed from the blood at the end of 45 minutes.

Dosage form. Sulfobromophthalein Sodium Injection, U. S. P., *ampuls*, 3%, 3 cc. (150 mg. of the dyo in 3 cc.).

LYMPHOGRANULOMA VENEREUM

LYMPHOGRANULOMA VENEREUM ANTIGEN (FREI ANTIGEN). Prepared from chick embryo tissue infected with lymphogranuloma venereum virus.

Dosage. Intracutaneously, 0.05 to 0.1 cc.; and similar injection of the control material. Cutaneous reaction to antigen and to control are made in 48 to 72 hours.

Dosage form. Package containing 1 cc. *ampul* of antigen and 1 cc. of control.

OPHTHALMIC LESIONS

FLUORESCEIN SODIUM, U. S. P. To demonstrate minute abrasions of the corneal and conjunctival epithelium. Areas denuded of their epithelial surface are stained a brilliant green and the area limits more easily seen. Also useful as a test for patency of the lacrimal duct, the stain appearing promptly in the nasal secretion if lacrimal drainage is normal.

Dosage. 0.5% *solution* instilled into conjunctival sac (2% solution may be used as indicated; must be washed out for proper observation). Denuded areas may be seen by gross inspection or more exactly under the slit lamp.

ROENTGENOGRAPHIC AGENTS

BARIUM SULFATE, U. S. P. Used in roentgen ray examination of gastrointestinal tract. Passes unchanged through the digestive tract. (Caution: "Barium sulfate" should always be spelled out completely to avoid confusion with the highly toxic soluble barium salts such as barium sulfide or barium sulfite.)

IODIZED OIL, U. S. P. Contains 33–42% organically combined iodine addition product of vegetable oil.

Action and uses. Injected as contrast medium in roentgen diagnosis, especially tumors of the spinal cord, localization of bronchial and pulmonary lesions, and in gynecology.

Caution. Iodized oil injection constitutes introduction of a foreign substance and possible irritant. Especial care should be exercised as follows: (1) Oils aged and darkened beyond normal color should not be used. (2) Subarachnoid injection should be avoided except when all other diagnostic measures fail. (3) In bronchography, introduction of the oil restricts the respiratory space, therefore its use should be avoided where such restriction is contraindicated. (4) Pressure should always be carefully controlled during injection. Intrauterine injection should never be made except under fluoroscopic observation. The oil should never be used intravenously.

Dosage. 1–5 cc. or more according to intended use.

venous injection of nontoxic soluble iodine compounds which are rapidly excreted in the urine. Sodium iodide, in the necessary dose, is too toxic for intravenous use.

If there be history of any allergy, a small initial dose should be given first. In any event, epinephrine hydrochloride 1:1,000 should always be available when the injection is made. Ocular, oral, and intradermal tests to detect sensitivity to intravenously administered iodine compounds are not reliable since reactions are more often due to a direct vascular effect. The intravenous use of these drugs is contraindicated in patients with severe liver disorders, nephritis, and severe uremia, and they should be used with caution in advanced tuberculosis and hyperthyroidism.

IODOALPHIONIC ACID, U. S. P.—(Priodax). Medium for cholecystography, taken orally. Excreted primarily through the kidneys.

Dosage. 3 Gm. (usual adult); more may be given. One 0.5 Gm. tablet every 5 minutes until 6 tablets have been taken; with several glasses water during or after light fat-free meal in late afternoon. No food until roentgenographic examination following morning.

IODOPYRACET, U. S. P. (Diodrast). Contains 61.5–63.5% iodine.

Dosage. Usually administered intravenously for urography. Usual adult dose is 20 cc. (7 Gm. of iodopyracet) given slowly; children are given correspondingly smaller doses.

Dosage form. Iodopyracet Injection, U. S. P. (Solution Diodrast) 35%, W/V: 10 cc., 20 cc., 30 cc. *ampuls.*

(Note: A 70% solution of this drug is also available for special diagnostic procedures such as angiography, angiocardiography, and cholangiography. Doses vary from 15 to 100 cc.).

SODIUM IODOMETHAMATE, U. S. P. (Neo-Iopax). Contains 50.5–52.5% iodine.

Dosage. For urography, 20 cc. containing 15 Gm. of sodium iodomethamate. Children are given correspondingly smaller doses.

Dosage form. Sodium Iodomethamate Injection, U. S. P. (Neo-Iopax Solution), *ampuls*, 10 cc. (0.5 Gm. per cc.), 20 cc. (0.75 Gm. per cc.).

TUBERCULOSIS

PURIFIED PROTEIN DERIVATIVE OF TUBERCULIN, U. S. P. (Tuberculin P. P. D.). Sterile, soluble product of the growth of the tubercle bacillus prepared in a special liquid medium free from protein. Amorphous, whitish powder, readily soluble in water.

Dosage. Diagnostic, 0.00002 mg. (first test dose), or 0.0002 mg. (second test dose).

Dosage forms. *Tablets*, Purified Protein Derivative of Tuberculin, First Strength, and Second Strength: packages of 2 vials (5 tests each) and 1 cc. ampul of sterile diluent; and packages of 10 tablets (100 tests) with 10 cc. of diluent.

soluble products of growth of the tubercle bacillus; contains about 50% glycerl

Dosage. Intracutaneous (Mantoux): 0.1 cc. of 1:10,000 solution (contai ing 0.01 mg.) injected intracutaneously and read in 48 to 72 hours. If negativ this may be followed by injection of 1:1,000 (0.1 mg.) or 1:100 (1 mg.) solutio Reaction usually reaches height in 48 hours.

Dosage form. *Vials*, various sizes.

TUBERCULIN PATCH TEST (VOLLMER). Consists of thin filter pap squares about 1 cm. area, which have been treated with tuberculin solution a dried. Two of these squares and a control square consisting of filter paper sa urated with glycerin broth are applied to the skin (forearm) after thorou cleansing with acetone, and attached to the skin with adhesive plaster. T patches are removed after 48 hours. If positive, there will be an eruption follicles or erythematous papules. In young children, or where sensitivity suspected, it is advisable to leave the patches on for about 6 hours, using t complete period if there is no reaction.

Dosage form. *Adhesive strips* in packages of 1, 10, and 100 tests.

DIURETICS AND ANTIDIURETICS

DIURETICS

Osmotic

AMMONIUM CHLORIDE, U. S. P. Colorless crystals or white powder; cool, saline taste. Soluble in water, 1:2.6; alcohol, 1:1,000; glycerin, 1:8.

Diuretic action. (See also "Cough Therapy.") Acid-producing diuretic, the ammonia changing to urea and the chloride to sodium chloride. Acidification used to combat bacterial infection in urinary tract; to combat alkalosis; synergistic to mercurial diuretics and to digitalis in clearing kidney and cardiac congestion and edema.

Toxicity. Care needed to avoid general acidosis.

Dosage. For acidifying urine, 1 to 2 Gm. 4 times daily, in enteric coated tablets to avoid gastric irritation. Its use alone for diuresis is not very practical, as it requires at least 8 to 12 Gm. daily, sometimes for several days.

Dosage form. Tablets, enteric coated, 0.5 Gm.

DEXTROSE INJECTION, U. S. P. 50%, 50 cc. administered intravenously, slowly, will often promote an adequate diuresis due to a strong osmotic action.

SODIUM CHLORIDE, U. S. P. Colorless crystals or white powder; saline taste. Soluble in water (1:2.8); glycerin, 1:10; slightly, in alcohol.

Diuretic Action. (See also "Parenteral Fluids.") Depends on concentration. *Isotonic Sodium Chloride Solution (0.9%)* gives slow, prolonged diuretic action; increases extracellular fluid volume, blood volume is increased, and serum protein concentration decreased, thus increasing glomerular filtration with resulting diuresis. Tubular activity is little affected. *Hypertonic sodium chloride solutions* give greater diuresis due to the additional factor of greater withdrawal of water to maintain osmotic equilibrium between intracellular and extracellular fluid.

Sodium chloride should be avoided in presence of clinical edema.

Xanthines

℉ See "Spasmolytics" for full description.

℞ Theophylline, theobromine and caffeine are diuretic in that order. Two are provided because tolerance does develop. A sodium-free theobromine salt is included for use in patients who need a diuretic and are on a low-sodium diet. Xanthines enjoy greatest usefulness in the relief of cardiac edema where kidney function is adequate. They are used also to supplement mercurial diuretics and digitalis.

AMINOPHYLLINE, U. S. P. 0.2 Gm. 3 or 4 times daily.

THEOBROMINE CALCIUM SALICYLATE, U. S. P. 0.5 to 1 Gm. three times daily.

Mercurial Diuretics

Mercurial diuretics essentially are methoxy-mercuripropyl derivatives of organic acids. Diuretic efficiency enhanced by theophylline and by acid salts such as ammonium chloride and ascorbic acid.

Actions and uses. Cause elimination of sodium as well as of water thus diminishing ability of body to retain fluid. Probably, by direct renal action; reducing the

Action in congestivo cardiac failure: Gradual fall in right auricular pressuro, and, in most patients, slow rise in cardiac output. As diuresis subsides, right auricular pressure tends to riso, but still considerably below initial levels, while cardiac output tonds to return to initial level.

Toxicity. Manifestations of sodium deficiency should bo watched for. Should be used with caution in tho presonce of renal insufficiency.

Over-diuresis and salt restriction. High blood urea nitrogen, low sodium level; weakness, lassitude, anoroxia, nausoa, vomiting, restlessness, thirst unrelieved by plain water, apathy, montal confusion, fall in blood pressuro, pulse rate accelerated, pulso volumo diminished, clammy skin, shock, coma.

Cerebral thrombosis has been precipitated in aged by dehydration due to morcurials.

Exercise care where thero aro severo bladder symptoms or over 60 cc. residual urino as acuto retention may result.

MERALLURIDE INJECTION, U. S. P. (Mercuhydrin.) Sterile solution of meralluride (methoxyoxymercuripropylsuccinylurea and theophylline in approximately molecular proportions) and just sufficient sodium hydroxide to effect solution. Contains, per cc., equivalent of 39 mg. mercury and 48 mg. theophylline.

Dosage. Give initial dose of 0.5 cc. intravenously or intramuscularly to test for idiosyncrasy; wait 24 hours. Usual dose is 1 cc. May be given twice weekly, or as may be indicated.

Dosage forms. *Ampuls*, 1 cc., 2 cc.

MERCAPTOMERIN SODIUM, N. N. R. (Thiomerin Sodium.) Disodium salt of N (γ-carboxymethylmercaptomercuri-B-methoxy) propyl camphoric acid. Solution contains 40 mg. of mercury per cc.

This preparation, which is given subcutaneously, is claimed to have less cardiac toxicity and less irritation at site of injection. Diuretic response to this drug *subcutaneously* is as satisfactory as the mercurials used intramuscularly or intravenously.

Dosage. 0.5 to 2 cc. subcutaneously. Powder is brought into solution with sterile distilled water.

Dosage forms. *Ampuls*, 1.4 Gm. of powder (10 cc.), 4.2 Gm. of powder (30 cc.).

ANTIDIURETICS

Antidiuretics are used to control polyuria, and are of primary importance in the management of the polyuria of diabetes insipidus. Lesions of the posterior pituitary gland impair the ability of the renal tubule to resorb water to maximum capacity. The posterior pituitary hormone given parenterally or by application to the nasal mucosa inhibits water diuresis but is ineffective against salt- or urea-induced diuresis.

POSTERIOR PITUITARY INJECTION, U. S. P. (See also under "Hormones and Synthetic Substitutes.") Contains 10 U. S. P. units of posterior pituitary per cc.

Dosage. 0.5 to 1 cc. intramuscularly or subcutaneously daily, or as necessary to control symptoms. Same dosage may be given on cotton pledgets inserted into nostrils for several minutes 2 or more times daily. Dry posterior pituitary powder (approximately 0.15 Gm.) applied to nasal mucosa has also been effective.

Chapter 13.

GASTROINTESTINAL DRUGS

ACIDS

DILUTED HYDROCHLORIC ACID, U. S. P. (10%). Colorless, odorless liquid. This is used as a physiologic substitute in patients with achlorhydria. It is usually administered in doses ranging from 2 to 8 cc. diluted in a glassful of water (200–250 cc.) with instructions to be consumed with meals. In order to avoid damage to the teeth, this diluted Diluted Hydrochloric Acid should be sipped through a glass tube.

GLUTAMIC ACID HYDROCHLORIDE, N. F. White powder; 1 gram is soluble in about 3 cc. of water; insoluble in alcohol. 0.3 Gm. equivalent to 0.6 cc. of diluted hydrochloric acid, U. S. P. This offers a more convenient form of correcting achlorhydria or hypochlorhydria. When it dissolves, free hydrochloric acid is liberated.

Dosage. Prescribed on the basis of diluted hydrochloric acid, U. S. P. equivalency.

Dosage form. *Capsule*, N. F., 0.3 Gm.

ANTACIDS

Antacids have been used in the management of gastrointestinal disturbances, since ancient days. Dr. Sippy's popularization of the use of antacids in peptic ulcer management has had a profound influence. As a result, the diagnosis of ulcer now usually means that one or another antacid will be given, regardless of whether there is excess gastric acidity or whether there is actual need for medication.

This widespread use of antacids demands that especial care be used in selecting safe as well as effective agents.

The ideal antacid neutralizes the effect of excess acidity without causing rebound acid secretion; allows normal digestion; causes no untoward systemic manifestations; and does not interfere with absorption of accessory food substances.

ALUMINUM HYDROXIDE GEL, U. S. P. White, viscous, aqueous suspension containing about 4% Al_2O_3 (about 6% ($AlOH_3$)), also as a white powder (Dried Aluminum Hydroxide Gel, U. S. P.) containing about 50% Al_2O_3 (about 76.5% $Al(OH)_3$). Administered orally, it effectively reduces both free and total acid of gastric contents, particularly when hyperacidity is present. This property makes it very useful in the symptomatic management of patients with peptic ulcers. Its main advantage over soluble alkalies is the absence of danger of alkalosis. It is somewhat constipating. It combines with insoluble phosphates, hence reduces phosphates available for absorption. Where intake is borderline, blood phosphates may be substantially reduced. (Aluminum phosphate gel does not possess this action). Aluminum Hydroxide Gel also is said to interfere with absorption of vitamin K, which would have significance in patients with bleeding ulcers.

The gel will neutralize to pH 3.6 about 12 times its volume of gastric juice containing 0.1N hydrochloric acid.

Dosage. 4 to 8 cc. in water or milk, every 2 or 4 hours, or 0.3 Gm. to 0.6 Gm. of the tableted dry powder.

Dosage forms.

Aluminum Hydroxide *Gel*, U. S. P.
Dried Aluminum Hydroxide Gel *Tablets*, U. S. P. 0.3 Gm., 0.6 Gm.

SODIUM BICARBONATE, U. S. P. White odorless powder soluble in water, 1:10. Incompatible with acids and acid salts and the salts of most alkaloids. 1 Gm. neutralizes 120 cc. of 0.1 N HCl.

Action and uses. Prompt in the relief of gastric hyperacidity. Used to combat systemic acidosis. Employed to render the urine alkaline, in the treatment of infections of the urinary tract. Used locally for various skin disorders and as an antipruritic. Because of its action as a mucus solvent sodium bicarbonate often is employed as an ingredient of mouth washes, douches, and enemata.

It is also of use to produce a gas bubble in the stomach, which, in fluorography of the heart, helps outline the lower left cardiac border in determining enlargement.

Toxicity. If the amount of sodium bicarbonate ingested is more than is necessary to neutralize the acid in the stomach at the time of administration, the excess will pass into the intestinal tract and contribute to a systemic alkalosis. It also produces the so-called "rebound" of acid secretion. Its reaction with HCl in the stomach produces carbon dioxide which may cause gastric distention (this may be dangerous if the patient has an ulcer near perforation). Avoid use in patients on low-sodium diet.

Dosage. *Gastric antacid:* 1 to 4 Gm., orally. For *systemic acidosis*, may be given intravenously (depending on the degree of acidosis). A safe average dose is 0.42 Gm. per kilo of body weight. As a *mucus solvent*, a 2 percent solution with 1 percent sodium chloride is used for irrigating the oral cavity and as a general "mouth wash."

Dosage form.

Tablets, U. S. P. 0.3 Gm., 0.6 Gm.
Ampuls, various sizes.

ANTIDIARRHEICS (NONSPECIFIC)

Agents used in the relief of diarrhea caused by dietary indiscretion and other nonspecific entities are the protectives, protective astringent, and opiate analgetic and antiperistaltic drugs. Adsorbents of various kinds have been used, but these may adsorb beneficial substances such as enzymes as well as the noxious substances.

The two simplest and usually effective agents are bismuth subcarbonate with or without morphine sulfate. Morphine sulfate is proposed rather than the traditional and unnecessarily complex Camphorated Opium Tincture ("Paregoric"), effect of which is due only to its morphine content.

BISMUTH SUBCARBONATE, U. S. P. White powder, odorless and tasteless. Insoluble in water and in alcohol.

Actions and uses. Acts as an astringent antidiarrheic and also has a slow antacid effect. Preferable to the subnitrate which may cause nitrite effects (q. v.)

1 Gm.

Dosage form. *Tablets*, U. S. P. 0.3 Gm.

MORPHINE SULFATE, U. S. P. (See "Analgetics", ch. 2, for full description.)

Action as antidiarrheic. (See "Analgetics", ch. 2, p. 83.)

Dosage as antidiarrheic. 1.6 mg. (content in 4 cc. of the Camphorated Opium Tincture) may be added to each dose of suspension of the bismuth subcarbonate. As a prescription, the drugs may be administered in a vehicle of peppermint or other aromatic water.

Dosage form. *Mixture:*

Bismuth Subcarbonate, 0.6 Gm. (or more)
Peppermint Water to 4 cc.
(Morphine sulfate 1.6 mg. per 4 cc., added when indicated.)

CATHARTICS

Cathartics promote evacuation of the bowels by increasing the fecal bulk or the fluid content or both, or by increased peristalsis. The site of main action may be the colon, small intestine, or both. Times of action range from 30 minutes to 16 hours with various preparations and patients. Three types of cathartics are included: (1) hydragogue, (2) irritant, and (3) mechanical and lubricant (emollient).

Hydragogue

MAGNESIA MAGMA, U. S. P. (Milk of Magnesia.) White, opaque, aqueous suspension of 7 to 8.5% of magnesium hydroxide. Stability affected by freezing and by temperatures above 35° C.

Actions and uses. Pleasant, mild saline cathartic. Also mild antacid effect. Cathartic effect in 1 to 2 hours.

Usual dose. Cathartic—Adult: 15 cc.; infants and children, 2 to 8 cc. *Antacid*—4 cc.

MAGNESIUM SULFATE, U. S. P. (Epsom Salt.) Colorless crystals, freely soluble in water (1:1). Saturated solution is 72% at 25° C.

Actions and uses. Cathartic, due to osmotic retention of fluid resulting in mechanical stimulation of bowel. Watery stool. Given in concentrated form it acts in several hours; well diluted, it acts in 1 to 2 hours.

Toxicity. Avoid where there is renal obstruction as accumulated salt may induce symptoms of magnesium poisoning. These symptoms also result from any other failure to excrete the salt.

Dosage. 15 Gm. (retains approximately 400 cc. of fluid in the intestinal tract). One teaspoonful of the salt contains about 8 Gm.

SODIUM PHOSPHATE, U. S. P. Colorless salt, soluble 1:4 in water; very slightly soluble in alcohol.

Actions and uses. Pleasant, saline cathartic, not as drastic as magnesium sulfate, hence safer to use. Four grams produces single soft (not liquid) stool in about 1 hour if taken on empty stomach.

Dosage form.

Crystals, U. S. P., 4 Gm. (1 teaspoonful, well filled)
Solution N. F., cc. (contains about 8 Gm. *sodii* in phosphate, U. S. P.)

CASCARA SAGRADA, U. S. P. One of the emodin catbartics whose active constituents are anthracene derivatives.

Actions and uses. Its irritant action stimulates the propulsive movements of the large intestines. Active principles of this drug are absorbed in part from the intestinal tract and excreted in body fluids.

One of the most extensively employed cathartics. Action is mild and unaccompanied by discomfort or griping. Therapeutic dose will cause a single evacuation of the bowel in approximately 8 hours with solid or semisolid stool.

Dosage.

Cascara Sagrada Extract: 0.3 Gm.

Aromatic Cascara Sagrada Fluidextract: 2 cc.

Dosage forms.

Cascara Sagrada Extract *Tablets*, U. S. P. 0.3 Gm.

Aromatic Cascara Sagrada *Fluidextract*, U. S. P.

CASTOR OIL, U. S. P. The irritant ricinoleic acid formed from saponification of this oil and intestinal contents so increases peristaltic and segmental activity of the small bowel that complete evacuation (semi-fluid) occurs in a few hours. Reduction of antiperistaltic activity of the colon facilitates the process. Some after-constipation may result due to completeness of evacuation.

Castor oil is used when prompt and complete emptying of the intestines is indicated. Because of the attendant hyperemia, it is contraindicated in pregnant and menstruating women.

Dosage. 15 to 30 cc. (usual dose: 15 cc.); infants: 4 cc.

Mechanical and Lubricant (Emollient)

LIQUID PETROLATUM, U. S. P. (Mineral Oil.) Colorless, transparent, oily liquid; odorless and tasteless. Insoluble in water and alcohol; miscible with most fixed oils, but not castor oil; soluble in volatile oils.

Actions and uses. Effect is mainly that of prevention of drying of feces in the colon. Its lubricant effect acts to facilitate defecation, hence of value for patients with heart disease and hemorrhoids.

Interferes with absorption of bile and fat-soluble vitamins (A, D, K) and drugs. Rectal use therefore *preferable to oral use to soften fecal matter.*

Dosage. Usual dose, 15 cc. Ten to thirty cc. may be given three times daily after meals or 30 to 60 cc. at bedtime.

Dosage forms.

Liquid Petrolatum.

Liquid Petrolatum Emulsion (50% in liquid petrolatum) for those unable to take oil. Emulsion contains a small amount (approximately 1%) of agar or other gum as an emulsifying agent only, *not* for therapeutic effect.

METHYLCELLULOSE, N. F. Grayish-white fibrous powder. Aqueous suspension neutral to litmus. Swells in water producing a clear to opalescent viscous colloidal solution. Insoluble in alcohol.

Actions and uses. In the treatment of constipation. Forms soft, gelatinous, water-retaining residue in lower bowel; protective action. Use with care to avoid dependence.

Dosage. See below.

Dosage forms. Methylcellulose Solution, 1%, containing methylcellulose yielding a viscosity of 4,000 centipoises. The effective dosage of this material

stituents, with a resultant increase in bile flow. *Hydrocholeretics* increase the volume of bile decreasing its viscosity without stimulating the formation of bile constituents.

The *natural bile acids* are *choleretics.* They are derivatives of cholanic acid, i. e., cholic acid (3,7,12 trioxycholanic acid) and desoxycholic acid (3,12 dioxycholanic acid). These acids occur in combination (conjugated) with the amino acids taurine and glycine.

Oxidized bile acids (oxidation of the cholanic acids to ketocholanic acids) are *hydrocholeretics.*

OX BILE EXTRACT, U. S. P. Dried alcoholic extract of ox bile. One gram represents eight grams of fresh bile, and contains approximately 0.24 Gm. each of sodium glycocholate and sodium taurocholate.

Bile is used to aid in the digestion and absorption of fats and of fat-soluble vitamins (A, D, K). Where there is an absence or deficiency of natural bile secretion into the intestine ox bile extract is useful as a substitute. Subsequent absorption of the bile salts present in the extract brings about choleretic action resulting in increased formation of bile constituents, bile fluids, and flow. Care should be exercised in giving this drug to patients with biliary obstruction as increased production and obstructed elimination of bile salts may lead to toxic blood levels.

Dosage. 0.3 Gm. repeated as necessary.

Dosage form. *Tablet,* U. S. P. 0.3 Gm., *enteric coated.*

DEHYDROCHOLIC ACID, N. F. This is a trikotocholanic acid made by oxidizing the cholanic (cholic) acids present in natural bile.

Dehydrocholic acid is hydrocholeretic in action and is used in conditions where increased bile *volume* (its effect on bile constituents is uncertain) is desired. It has been used for this effect in the postoperative management of bile tract surgery, such as promotion of drainage of an infected common bile duct. It should not be used where there is complete biliary obstruction. It is mildly diuretic.

Dosage. 0.25 to 0.5 Gm. three times daily after meals for four to six weeks.

Dosage form. *Tablets,* N. F. 0.25 Gm.

Hematics, (agents affecting the blood), include (1) antianemia drugs, and (2) congulant and anticoagulant drugs.

ANTIANEMIA DRUGS

Antianemia drugs are used to correct acquired specific deficiencies which have resulted in clinically significant diminution of available circulating hemoglobin.

Since the *adequacy of present diagnostic measures makes therapeutic trial* unnecessary, the first step in the appropriate use of antianemia drugs is definitive diagnosis. Then, treatment involves giving iron for iron deficiency anemias; liver extract (or its essential elements) for macrocytic anemias; both for coexisting primary and secondary anemias; and detecting and eliminating exogenous factors.

Iron

Iron is valuable only in correcting those anemias caused by iron deficiency, such as result from chronic hemorrhage, blood loss, blood destruction, toxic renal and liver diseases, or inadequate dietary intake of iron. Nutritional anemias are most common in infancy, childhood, and during pregnancy.

Inorganic iron preparations apparently are more effective than are the organic; and bivalent salts usually are more effective than the trivalent. The utilization of iron from forms such as reduced iron, ferrous carbonate, and ferric ammonium citrate is comparatively low (in spite of relatively high iron content), often requiring undesirably large doses. With insoluble substances *such as* reduced iron, and ferrous carbonate, the acidity required to render them soluble often is lacking or diminished in anemia; large doses are necessary to compensate.

Toxicity and side effects. Untoward effects of the ferrous salts such as ferrous sulfate are relatively infrequent and if present are chiefly gastrointestinal: cramps, diarrhea (slight constipation is more common). May be overcome by adjusting dose to point of tolerance or if indicated, by rest period of a day or so. Iron medication colors feces black.

Dosage. Daily *utilization* of approximately 25 mg. of iron is required to raise hemoglobin 1% per day. This is furnished by a daily dose of 1 Gm. of ferrous sulfate or 0.6 Gm. of exsiccated ferrous sulfate, each of which has a metallic iron content of 180 mg. The optimum therapeutic dose of iron, for some unknown reason, is far in excess of the calculated iron deficiency.

After correction of the clinical deficits, diet deficiency anemias should be approached from the dietetic point of view, rather than continued administration of iron preparations. *Foodstuffs high in iron content are eggs, apricots,* blackstrap molasses, meat, liver, peas, beans.

FERROUS SULFATE, U. S. P. ($FeSO_4.7H_2O$). Pale, bluish green crystals or granules; odorless; saline, styptic taste. Efflorescent in dry air; exposed to moist air, crystals rapidly oxidize to brownish yellow basic ferric sulfate, which should not be used. Iron content, approximately 20%. Soluble in water, 1: 15; insoluble in alcohol.

Dosage. 1 to 2 Gm. daily *as* enteric coated tablets, *in divided doses,* after meals (minimize gastric irritation). Children, 0.6 to 0.8 Gm. daily; Infants, 0.4

(If Exsiccated Ferrous Sulfate, U. S. P. is used, 0.2 Gm. of that salt approximately is equivalent to 0.3 Gm. of the hydrated salt, Ferrous Sulfate, U. S. P.)

Dosage forms.

Tablet, U. S. P., 0.3 Gm. (Ferrous Sulfate, U. S. P.), enteric coated.

Ferrous Sulfate *Syrup* (or *Elixir*) (for administration to children unable to take tablets): contains approximately 0.16 Gm. per cc. Usual dose, according to deficiency: children, 16 to 20 cc. daily; infants, 10 to 12 cc. daily; in 3 divided doses, after meals.

Liver and Stomach Preparations

Liver and stomach preparations primarily are intended for the treatment of pernicious anemia (hyperchromic macrocytic). The U. S. P. unit of liver or of stomach is defined by the U. S. P. Antianemia Preparations Advisory Board as that amount of the product which produces, when administered daily, clinical and hematopoietic responses in Addisonian pernicious anemia, that are considered by the Board to be satisfactory. Oral preparations of liver are less efficient than the injectable and therefore are not included. Powdered stomach, administered orally only, is included for patients who are unable to receive liver therapy, due to sensitivity or other causes, or for whom a combination of liver and stomach therapy seems desirable.

LIVER INJECTION, U. S. P. Sterile, aqueous solution of that soluble thermostable fraction of mammalian livers which increases the number of red blood corpuscles in the blood of persons affected with pernicious anemia. Contains either 10 U. S. P. units or 15 U. S. P. units, injectable, in each cc.

Actions and uses. To stimulate erythrocyte maturation in hyperchromic macrocytic anemia and in certain other macrocytic anemias. Reticulocytes rise from normal (1% or less) to 15% or more in 5 to 10 days; return to original level in about 16 days when restoration of mature red cells is half completed. Improvement in about 10 days and nearly normal within 3 weeks. Megaloblastic hyperplasia of bone marrow recedes to normal.

Also effective in sprue and useful in pellagra, anemia from tapeworm infestation, and other diseases characterized by macrocytic anemia.

Dosage. Varies from patient to patient. For average patient in relapse, 15 units, or more daily intramuscularly, for 3 to 4 days; 15 units 2 or 3 times weekly until reticulocytes return to normal and erythrocytes begin to increase; then 15 units once or twice weekly until blood is normal. Maintenance: approximately 15 units every 2 to 3 weeks. If neurological complications, vigorous treatment is indicated, using 2 to 3 times the amount needed to keep blood picture normal. Response is only guide as to dosage.

Dosage forms. *Injection*, U. S. P., *ampuls*, 10 cc., 15 units per cc. (Strength greater than 15 units per cc. not presently assigned by the Board, due to possible loss of unknown factors by further concentration.)

POWDERED STOMACH, U. S. P. Dried and powdered defatted wall of hog stomach. Activity rapidly destroyed if suspended in hot liquid.

Actions and uses. In treatment of pernicious anemia.

Dosage. Average daily dose not less than amount (approximately 40 Gm.) furnishing 1 U. S. P. oral unit (amount of oral material required to give satisfactory response). Larger doses may be needed in relapse and in severe or complicated cases. May be [illegible]

FOLIC ACID, U. S. P. (also referred to as "vitamin M," "L. casei factor," "*vitamin B_c*"; *pteroylglutamic acid*). Yellowish, odorless, crystalline powder. Insoluble in water or in alcohol. Readily dissolves in dilute solutions of alkali hydroxide and their carbonates.

Actions and uses. Produces response similar to that of liver extract, in pernicious anemia, sprue, nutritional macrocytic anemia. It probably does not prevent or cause improvement in spinal cord lesions; *folic acid* is therefore only an adjunct to liver therapy.

Dosage. 5 to 10 mg. daily, orally. Parenteral administration has no advantage.

Dosage forms. *Tablets*, U. S. P. 5 mg.

Vitamin B_{12}

VITAMIN B_{12}, U. S. P. Cobalt-containing substance usually produced by the growth of suitable microbial organisms (chief source, *Streptomyces griseus*), or obtained from liver (yield is low). Dark red crystals or powder. Anhydrous compound very hygroscopic. Soluble in water, 1:80; soluble in alcohol.

Actions and uses. Has hemopoietic activity apparently identical with antianemia factor of liver, but not yet established as its complete or essential counterpart. Effective in pernicious anemia (with or without related neurologic disorders), sprue, nutritional macrocytic anemia, and certain cases of megaloblastic anemia of infancy. Particularly useful for patients sensitive to liver extract. *Folic acid may be given with Vitamin B_{12} according to individual response.*

Dosage. Minimum, approximately 1 microgram daily. One microgram presently estimated to be equivalent to one U. S. P. unit of parenteral liver, but further study needed to determine accurate comparative clinical potency.

Pernicious anemia in relapse. 15 to 30 mcg. once or twice *weekly* until remission. Average maintenance: 15 to 30 mcg. at *15- to 30-day* intervals. *Sprue:* 15 to 30 mcg. once or twice a week; 15 mcg. weekly thereafter often necessary to prevent relapse.

Dosage forms. Various size *ampuls* containing 15 mcg and 30 mcg per cc.

COAGULANTS AND ANTICOAGULANTS

Coagulants

Coagulation mechanism. Prothrombin (in the blood) + calcium + thromboplastin (thrombokinase) = Thrombin.

Thrombin (fibrin ferment) + fibrinogen (in the blood) = fibrin (blood clot).

Hemostatics

ABSORBABLE GELATIN SPONGE, U. S. P. (Gelfoam). Sterile, absorbable, water-insoluble gelatin-base sponge. Insoluble in aqueous media but absorbable in body tissues.

Actions and uses. To control capillary bleeding particularly when moistened with thrombin; check oozing from the dura, lacerations of dural venous sinuses, bleeding in tumor beds, lacerations of the liver and other organs. May be used as a surgical sponge and left in place following operative wound closure. Is completely absorbed in 4 to 6 weeks.

Dosage. Moisten with isotonic sodium chloride solution, or thrombin solution (q. v.) and apply to bleeding surfaces.

thromboplastin in presence of calcium.

Actions and uses. Aids coagulation by supplementing thromboplast
by disintegration of tissue elements at site of hemorrhage. Apply *topi*
(*should never be injected*) to check capillary bleeding; nosebleed; followi
of the bones, glands, nose, throat, mouth.

Dosage. Apply as dry powder or 1,000 to 2,000 units dissolved
isotonic sodium chloride solution.

Dosage forms. *Vials* of 1,000 2,500, 5,000 units of sterile powder;
with isotonic sodium chloride solution.

Vasoconstrictors

EPINEPHRINE AND PHENYLEPHRINE (q. v.).

Systemic Agents

VITAMIN K (q. v.).

Anticoagulants

Anticoagulant drugs are used to prevent intravascular clotting a
same time to avoid spontaneous bleeding. Drugs in this group shoul
with special care from the standpoint of toxicity and contraindicati
over-all mortality attributable to bishydroxycoumarin toxicity is about

Contraindications. Patients with blood dyscrasias characterized b
tendencies, such as hemophilia; after recent operations such as on
spinal cord; after recent intracranial hemorrhages, where a small a
bleeding may be serious; before surgery; threatened abortion; last 6
pregnancy.

BISHYDROXYCOUMARIN, U. S. P. (Dicumarol). 3,3′-Methyl
hydroxycoumarin). White or creamy white powder. Faint, pleas
slightly bitter taste. Insoluble in water and in alcohol. Slightly
chloroform; readily soluble in fixed alkali hydroxide solutions.

Actions and uses. Exact mode of action not known but assumed
liver to retard prothrombin production. Causes lengthening of pr
time by decreasing blood prothrombin concentration. Effect in 12 to
persisting 24 to 72 hours or more after discontinuance.

Prophylaxis and treatment of intravascular clotting, postoperative
phlebitis, pulmonary embolism, acute embolic and thrombotic occlusion
eral arteries, recurrent idiopathic thrombophlebitis and phlebothrom
does not affect thrombi or emboli already present, nor does it increas
blood supply of an area so affected. Dicumarol can only be expected
further intravascular clotting.

Bishydroxycoumarin has advantage over heparin in that it may
orally, but its action is slower and extends for longer period after disc
(heparin action is prompter and lasts only 4 to 6 hours). Therefor
cases both drugs are used, heparin being used for prompt action until bi
coumarin becomes effective. Pain at site of injection is another dis
of heparin.

Dosage. *On first day* determine prothrombin time to make certai
abnormally high. Give one dose of 200 to 300 mg. depending on size
tion of patient. *On second day,* if prothrombin activity is more than

activity drops to a dangerously low level, or if signs of bleeding appear, give Vitamin K_1 *intravenously* (1 Gm. *in emulsion form: 1 Gm.* K_1 *is dissolved in 25 cc.* alcohol, boiled down to approximately 15 cc. and suspended in 200 cc. of 5% dextrose.) If patient shows signs of shock or bleeding, whole blood transfusions are indicated.

Dosage forms. *Capsules*, U. S. P. or *tablets*: U. S. P. 25 mg., 50 mg., 0.1 Gm.

HEPARIN SODIUM, U. S. P. (Heparin). Mixture of active principles which prolong clotting time. Usually obtained from livers or lungs of domesticated mammals used for food by man. White, or pale-colored powder. Odorless or nearly so; hygroscopic. Soluble in water, 1:20. Potency is 100 U. S. P. Heparin Units per mg. One mg. keeps 500 cc. plasma liquid for approximately 4 hours. Considered to be a dextrorotatory polysaccharide made up of hexosamine and hexuronic acid units containing sulfuric acid ester groups.

Actions and uses. Inhibits blood coagulation. Little known about metabolism, excretion and fate of heparin in the body. Anticoagulant action appears to be effected by action on thrombin. Uses, same as bishydroxycoumarin (q. v.), but in contrast to it, effects are immediate and last only 4 to 6 hours.

Dosage. Usually intramuscularly. On occasion, intravenously, such as cardiac catheterization and in continuous intravenous drip to prevent clotting at tip of needle. Clotting time should be maintained between 15 and 20 minutes, and infusion adjusted accordingly. If chill or spontaneous bleeding occurs, discontinue drug.

Interrupted Dose: 50 mg. (5,000 units) may be administered at 4-hour intervals up to a total of 250 mg. per day.

Continuous Drip: 100 to 200 mg. (10,000 to 20,000 units) is added to 1,000 cc. of 5% sterile dextrose or isotonic sodium chloride solution. The flow may be started at about 20 drops per minute. Heparin overdose may be counteracted by the use of protamine sulfate.

Dosage forms. *Injection*, U. S. P., *ampuls:*

4 cc., containing 40,000 units (400 mg.).
10 cc., containing 10,000 units (100 mg.).
10 cc., containing 50,000 units (500 mg.).

HEPARIN SODIUM, REPOSITORY FORM, N. N. R. This is heparin sodium solution of 200 mg. per cc. in which is included 180 mg. of gelatin and 80 mg. of dextrose to slow absorption and prolong anticoagulant effect.

Dosage. Subcutaneous or intramuscular. The normal coagulation time should be determined before therapy and every 12 hours during first 48 hours of therapy, and every 24 hours thereafter to determine time and size of subsequent doses.

Initial dose, patients weighing up to 200 pounds: 1 cc. of repository heparin and 1 cc. of repository heparin with vasoconstrictors, to give a total of 400 mg. of heparin sodium. Dose is repeated about every 24 hours as determined by blood coagulation time.

Dosage forms.

Repository Heparin Sodium, N. N. R., 20,000 units (200 mg.) heparin sodium, 180 mg. gelatin, 80 mg. dextrose, 1 cc. *ampuls.*

Repository Heparin Sodium with Vasoconstrictors, N. N. R., 20,000 units (200 mg.) heparin sodium, 1 mg. epinephrine, 10 mg. ephedrine, 180 mg.

HISTAMINE-ANTAGONIZING AG

It has been shown that histamine plays an important role in aller
Numerous compounds have been developed which are described
antagonists and which relieve symptoms of certain allergic conditio
an accompanying spasmolytic effect principally in the reduction of br
Musculotropic and neurotropic effects in antagonizing acetylcholine
action on the gastrointestinal tract have also been demonstrated,
sufficient clinical evidence of the usefulness of this group in gastrointe

The following is quoted from New and Nonofficial Remedies, 195
Pharmacy and Chemistry of the American Medical Association: "
histaminic drugs produce undesirable side reactions. The incidence
of these toxic actions and the dose required to produce them vary wit
People differ in sensitivity to the toxic actions of the group as a wh
in their response to particular drugs. Thus, one may tolerate a dr
a high index of toxicity better than one which has a lower index."

Untoward Actions of the Group

Somnolence is the most common side action. Lack of coordinati
and inability to concentrate occur in varying degrees. For this rea
are cautioned against driving automobiles or operating hazardous ma
taking these drugs. Gastric complaints occur also, as do dryness o
throat, and nose. Since blood dyscrasias have occurred, and other
may be revealed after greater experience with these drugs, it is ad
indiscriminate or continuous use be avoided unless the patient
periodically.

Attention has been called [1] to the effect of diphenhydramine (b
tripelennamine (pyribenzamine) in inducing seizures in epileptic pa
focal lesions of the cerebral cortex. Tripelennamine (pyribenzami
petit mal seizures, while diphenhydramine (benadryl) has decreas
quency. Care should be exercised in giving these drugs to patients wi
disorders.

Choice of Drug

In view of the number of compounds being introduced as histamine-
agents, their evaluation is difficult at this time. There appears to b
significant difference among those in common use, with respect to eff
relief of symptoms. As for side effects, these appear to be significa
in both frequency and severity in the case of Thonzylamine. Pen
authoritative clarification of the status of these drugs, it is recommo

1. Tripelennamine Hydrochloride, U. S. P. (Pyribenzamine Hy
or Diphenhydramine Hydrochloride, U. S. P. (Benadryl Hydrochlo
as the basic drug in this group;

[1] Churchill, John A., and Gammon, George D.: The Effect of Antihistaminic Drugs
Seizures. J. A. M. A. 141:18 (Sept. 3) 1949.

R.) be tried if there is unsatisfactory clinical response to tripelennamine or to diphenhydramine.

DIPHENHYDRAMINE HYDROCHLORIDE, U. S. P. (Benadryl Hydrochloride). This is a white, crystalline powder having a characteristic odor and a bitter taste. It is very soluble in water, freely soluble in alcohol.

Diphenhydramine has antihistaminic effect, and indirect spasmolytic effect on the bronchi in certain allergic states. Its principal side effect is somnolence in 30 or 40 percent of patients.

Dosage. Average adult dose is 50 mg. 3 or 4 times daily, but the smallest effective dose should be used. Usually a minimum daily maintenance dose may be established after relief of acute symptoms. Caution is necessary in giving sedatives to patients receiving this drug. *Children's dose:* 10 mg. *Infant dose:* 2 to 5 mg., increase as necessary.

Dosage forms.

Capsule, U. S. P. 25 mg.; 50 mg.

Elixir, 10 mg. per 4 cc.

TRIPELENNAMINE HYDROCHLORIDE, U. S. P. (Pyribenzamine Hydrochloride). This is a white, crystalline powder having a bitter taste. It is very soluble in water and is soluble in alcohol.

Tripelennamine hydrochloride is a very efficient histamine antagonist whose somnolent effect is said to be less than that of diphenhydramine (benadryl) hydrochloride.

Dosage. Begin with 50 mg. orally, 4 times daily, preferably after meals. Reduce dosage as indicated. Dose for children is one-half the above adult dose; and for young children, dose according to relative weight.

Dosage forms.

Tablet, U. S. P. 50 mg. (scored in half).

Elixir, (Tripelennamine Citrate) 20 mg. per 4 cc.

THONZYLAMINE HYDROCHLORIDE, N. N. R. (Neohetramine, N. N. R.). This is a white, crystalline powder having a faint odor. It is very soluble in water, freely soluble in alcohol.

Thonzylamine hydrochloride appears to be as active, therapeutically, as the other drugs in this series. Current experience seems to indicate that its toxic effects are significantly reduced in frequency and severity.

Dosage. Average adult dose 50 to 100 mg.

Dosage forms.

Tablets N. N. R., 50 mg.

Syrup, N. N. R., 25 mg. per 4 cc.

DIMENHYDRINATE, N. N. R. (Dramamine). Although the specific clinical application of Dimenhydrinate (Dramamine) has been in the prophylaxis and treatment of motion sickness, it belongs to the group of histamine antagonists. Therefore it is discussed at this point.

The efficacy of Dimenhydrinate in the prevention and treatment of motion sickness was established as a result of a study by L. N. Gay and P. E. Carliner on a group of soldiers being transported by ship from New York to a port in Germany.

studies may establish the effectiveness of other antihistaminic drugs in motion sickness.

Precautions. Dimenhydrinate may give the same somnolent effect as other antihistaminic drugs and patients should be warned about operating motor vehicles and other machinery if drowsiness occurs.

Dosage. For prophylaxis and treatment, 50 mg. before meals and at bed time. For seasickness, initial dose is taken 30 minutes before boat leaves; for air and car sickness, 10 minutes before departure.

Dosage forms. *Tablets*, N. N. R. 50 mg. (scored in half).

Chapter 16.

HORMONES AND SYNTHETIC SUBSTITUTES

Hormones, the products of endocrine glands, act as regulatory and coordinating agents in respect to physical structure or organization of cells. They may be considered as falling into two main categories: first, those produced by the various ductless glands, and second, the tropic hormones originating in the anterior pituitary and acting as regulators of hormone production in the other ductless glands.

Chemically, the hormones fall into three groups, as follows: (1) *Protein hormones*—adrenal medullary, pancreatic islet, parathyroid, anterior pituitary, posterior pituitary, thyroid; (2) *Steroid hormones*—adreno-cortical, ovarian, testicular; (3) *Combined protein and steroid hormones*—placental.

As to source, there are both natural and artificial hormones. The artificial hormones are always synthetic, and some of the natural hormones may be prepared synthetically. For example, estradiol occurs naturally and also may be synthesized. Diethylstilbestrol, although synthesized, is an artificial estrogen since it does not occur naturally.

Therapy with hormones, though well established in conditions such as thyroid and pancreatic hormone deficiency, is still in somewhat of a state of confusion. Care is required in the evaluation of various claims, since established and consistent results have been observed in a limited number of conditions. The selection of hormones for therapeutic use has, as far as possible, been made on the basis of well-accepted use.

ADRENAL CORTEX

Electrolyte, water, and carbohydrate metabolism are disturbed by adrenal cortex insufficiency. Parenteral adrenal cortex extracts capable of overcoming this hypoactivity have been prepared. In addition, crystalline steroid compounds, particularly desoxycorticosterone, have been isolated from the cortex. Desoxycorticosterone appears to adjust imbalance in electrolyte and water metabolism.

With the isolation of the adrenocorticotrophic hormone (ACTH) from the pituitary, the regulatory action of the pituitary on the adrenal cortex has acquired increasing significance.

ADRENAL CORTEX EXTRACT, N. N. R. Extract of adrenal glands from domesticated animals used as food by man. It contains the cortical steroids essential for the maintenance of life in adrenalectomized animals.

Actions and uses. In treatment of Addison's disease or of other types of adrenal insufficiency. Exerts an effect on all three factors—electrolyte, water, and carbohydrate metabolic imbalance. Contrast with desoxycorticosterone acetate, which is limited to effect on electrolyte and water metabolism.

in Addison's disease, 500 dog units or more, daily; large [illegible] medication with larger quantities of sodium chloride or other sodium salts is of value.

Dosage forms. Adrenal Cortex Extract *Solution*, 10 cc. and 50 cc., 50 dog units per cc. (not more than 3 mg. of gland extractives).

DESOXYCORTICOSTERONE ACETATE, U. S. P. Steroid isolated from the adrenal cortex.

Actions and uses. Known activity limited to sodium, potassium, and water metabolism; increased retention of sodium ion and water, and increased excretion of potassium. It has no known effect on carbohydrate or protein metabolism. It has been effective in some cases of adrenal insufficiency where carbohydrate metabolism has not been impaired. Therapeutic doses restore serum sodium and potassium, and plasma volume to normal. Blood pressure is elevated.

Toxicity. Excessive dosage results in edema, pulmonary congestion, cardiac dilatation and failure. Arterial hypertension develops in about 30 percent of those under treatment for several months or years.

Dosage. Maintenance, 1 to 7 mg. daily. The higher the salt intake the lower the dosage required. Most patients will respond adequately to 3 mg. daily together with 3 to 6 Gm. of sodium chloride in addition to the amount in the diet.

Acute adrenal crises, 10 to 15 mg. may be needed twice daily for 1 or 2 days, together with liberal amount of adrenal cortex extract and 1 or 2 daily infusions of 1,500 cc. 5% dextrose in isotonic sodium chloride solution.

Dosage forms. 1 and 10 cc. *ampuls*; 5 mg. per cc., in sesame oil; subcutaneous or intramuscular.

OVARY

The estrogens and progestogens are the two main groups of hormones secreted by the ovary. Their production is linked with the regulatory action of the anterior pituitary gonadotropic hormones. Basophil cells in the anterior pituitary produce a follicle-stimulating hormone (FSH) which brings about growth of the follicle and the production of estrogen; a luteinizing hormone (LH) which induces ovulation, the formation of the corpus luteum, and the subsequent production of progesterone; and a lactogenic hormone.

Estrogens

Alpha-estradiol is considered to be the primary hormone secreted by the ovary. It is broken down in the uterus, placenta, and elsewhere, to form estrone, which is less active than estradiol; and estriol, which is less active than estrone parenterally but, in contrast, is active by mouth.

Actions. Role in endometrial cycle; maintenance of normal size and functional capacity of the uterus, fallopian tubes and vagina; promotes growth of the duct tissues of the breast; maintains normal condition of nasal and oral mucous membrane; acts on the pituitary to inhibit FSH and stimulate LH; in large doses, tends to suppress lactation by inhibiting anterior pituitary lactogenic hormone.

Carcinogenicity. The development of mammary carcinoma in animals having inherited sensitivity, has led to caution in use of estrogens in women who have family or personal history of mammary or genital carcinoma.

Uses. Menopausal disorders; senile vaginitis; essential dysmenorrhea; premenstrual tension; hypogenitalism in the female.

(1) *natural* estrogens (estradiol, estrone, estriol, water insoluble estrogenic substances, water soluble estrogenic substances) and (2) *artificial* estrogens (diethylstilbestrol and similar artificial products). There is a large number of commercial products in each category, many differing only in name. Diethylstilbestrol, U. S. P., and Conjugated Estrogenic Substances, N. N. R., have been selected for estrogenic therapy. Both drugs serve the same purposes, and they are provided as alternatives for each other to take care of idiosyncrasies which may be encountered for one or the other.

Oral therapy should prove adequate. Diethylstilbestrol vaginal suppositories are provided for use in patients for whom oral therapy is not feasible.

CONJUGATED ESTROGENIC SUBSTANCES, N. N. R. (Marketed as Amnestrogen, Conestron, Premarin, all N. N. R.) This is an amorphous preparation containing the naturally occurring, water-soluble conjugated forms of the mixed estrogens obtained from urine of pregnant mares. Sodium estrone sulfate is the principal estrogen present. Varying small amounts of other equine estrogens and relatively large quantities of nonestrogenic material are also present in the mixture. Total estrogenic potency is expressed in terms of an equivalent quantity of sodium estrone sulfate.

Actions and uses. See introductory statement.

Dosage. *Menopausal symptoms:* 1.25 mg. daily. If response is not satisfactory after a few days, dose may be increased. After symptoms are under control, dosage usually may be reduced. Cyclic administration 20 days per month preferred. Usually administration for 3 to 4 months is sufficient. *Senile vaginitis, kraurosis vulvae, pruritis vulvae:* 1.25 to 3.75 mg. daily. *Breast engorgement:* 3.75 mg. every 4 hours for five doses; or 1.25 mg. every 4 hours for 5 days.

Dosage form. *Tablets,* N. N. R., 0.3 mg., 0.625 mg., 1.25 mg., 2.5 mg.

DIETHYLSTILBESTROL, U. S. P. (Stilbestrol). This is one of the group of stilbene compounds found to possess estrogenic activity. It is a complete synthetic and artificial estrogenic compound. Chemically, it is a,a′-Diethyl-4,4′-stilbenediol. White, odorless powder. Almost insoluble in water; soluble in alcohol, fatty oils.

Actions and uses. Highly active by mouth as well as parentorally. Side reactions, particularly nausea, vomiting, and headache, have occurred frequently. These are believed to be due to its rapid absorption into the blood stream. Initial small doses to tolerance usually overcomes the difficulty. Toxicity probably no greater than with natural estrogens.

Dosage. *Menopausal symptoms:* 0.5 mg. to 1 mg. daily, by mouth; small doses initially if discomfort develops. After symptoms are under control, dosage usually may be reduced. Cyclic administration 20 days per month preferred. Usually, administration for 3 to 4 months is sufficient. *Senile vaginitis, kraurosis vulvae, pruritus vulvae:* 0.5 mg. to 1 mg. daily, by month; smaller doses initially if discomfort develops. *Suppression of lactation:* 5 mg. once or twice daily for 2 to 4 days.

The Council on Pharmacy and Chemistry, A. M. A., states: "There appears to be no evidence that enteric coated forms [diethylstilbestrol and digitalis] are superior to the plain dosage forms either from the standpoint of stability, therapeutic efficiency, or incidence of toxicity symptoms." (New and Nonofficial Remedies, 1951, p. xxxix.)

Progesterone, secreted by the corpus luteum, plays a definite role in the menstrual cycle and in the preparation of the endometrium for the fertilized ovum. It is initially secreted by the corpus luteum and later by the placenta, if pregnancy occurs. It is changed in the body to pregnanediol which, in combination with sodium and glycuronic acid, is excreted in the urine.

Therapeutically, progesterone has been used for a number of conditions such as primary and secondary amenorrhea, threatened or habitual abortion, dysmenorrhea, menorrhagia, etc. Its effectiveness in these conditions has not been satisfactorily established. Some value is claimed in the treatment of functional uterine bleeding. It is therefore difficult to set forth any definite recommendation for the use of this drug at this time. Preparations are listed for informational purposes.

PROGESTERONE, U. S. P. White powder, odorless, stable in air. Soluble in alcohol; sparingly in vegetable oils.

Dosage. 5 to 20 mg. intramuscularly daily.

Dosage forms. Progesterone *Injection*, U. S. P.: *ampuls*, various sizes.

ETHISTERONE, U. S. P. (Anhydrohydroxyprogesterone). White or slightly yellow powder; odorless, stable in air. Affected by light.

Ethisterone is the form of progesterone used for oral administration.

Dosage. 10 mg.

Dosage forms. Ethisterone *Tablets*, U. S. P.: 10 mg.

PANCREAS

Insulin is the antidiabetic hormone produced by the beta cells of the islet tissue of the pancreas. It is extracted commercially from beef or pork pancreas.

Actions and uses. Regulation of diabetes mellitus. One unit of insulin promotes the metabolism of approximately 1.5 Gm. of dextrose.

Toxic reactions. Insulin reaction—This term refers to the effects of hypoglycemia resulting from excessive action of insulin. The insulin reaction is by far the commonest complication of insulin therapy. Insulin reaction usually may be avoided by careful regulation of the dose of insulin, the intake of food and the amount of exercise.

Insulin allergy—Local reactions about site of injection of insulin, believed to be due to its antigenic property as a protein substance are encountered rather frequently.

Insulin fat atrophy—Wasting of subcutaneous adipose tissue about the sites of injection of insulin is observed most frequently in diabetic children and in female patients. The cause is unknown.

Insulin fat hypertrophy—Instances of local hypertrophy of subcutaneous adipose tissue in regions where insulin is injected regularly over long periods are observed.

Insulin edema—A generalized edema is observed fairly often in emaciated patients suffering from severe diabetes when the disease is brought under control rapidly.

Insulin presbyopia—Temporary loss of near vision due to rapid control of intense diabetes.

Insulin resistance—Rarely, cases of diabetes have been found in which the daily injection of several hundred units of insulin has not sufficed to control the

"regular" or "unmodified."

Actions and uses. Injected subcutaneously, it is absorbed rapidly. Blood sugar begins to fall rapidly, reaches a minimum in about 3 hours, then begins to rise, reaching a starting level in 6 hours. May be given subcutaneously or intravenously.

The action of the amorphous and of the zinc-insulin types are identical. The zinc-insulin injection may be used for patients who may be expected to exhibit allergic reactions to insulin.

Dosage. Usually injected 30 minutes before meals. Suggested dosage formula: Average grams of dextrose excreted divided by 1.5 gives the number of units usually adequate to abolish the glycosuria. Daily dose may be given in two portions, before breakfast and before supper.

Dosage forms. 10-cc. *ampuls* containing 20, 40, 80, 100 units per cc.

Storage. Above 0° C., but not above 15° C. Potency period: 2 years after removal from manufacturer's storage.

PROTAMINE ZINC INSULIN INJECTION, U. S. P. Sterile suspension of insulin modified by the addition of zinc chloride and protamine (polypeptide obtained from fish sperm.)

Action and uses. Blood sugar lowering action is prolonged and has its greatest effect in about 12 to 24 hours after injection. Injected subcutaneously only.

Dosage. One dose daily (subcutaneously only) usually adequate. Initial dose from about ⅔ to same dose as insulin. Administered in the morning, about 30 to 90 minutes before breakfast. Shake *carefully* before administration.

Dosage forms. 10 cc. *ampuls* containing 40, 80 units per cc.

Storage. Above 0° C., not above 15° C. Potency period 18 months after removal from manufacturer's storage.

Mixtures of insulin and protamine zinc insulin. By varying the proportions of soluble to protamine zinc insulin, clinical effects intermediate between those of the two kinds alone may be obtained. For example, NPH insulin, a 2:1 mixture of insulin and protamine zinc insulin, provides effects within 2 hours reaching maximum 7 to 11 hours after injection.

GLOBIN ZINC INSULIN INJECTION, U. S. P. Insulin modified by the addition of zinc chloride and globin (from hydrolysis of beef hemoglobin).

Action and uses. Maximum effect 8 to 16 hours after injection; intermediate between insulin and protamine zinc insulin. Injected subcutaneously only.

Dosage. Starting dose ⅔ to ¾ total daily dose of insulin; increased slowly as needed.

Dosage forms. 10 cc. *ampuls* containing 40, 80 units per cc.

Storage. As for Protamine Zinc Insulin.

PITUITARY

See "Oxytocics" and "Antidiuretics."

PLACENTA

The chorionic gonadotropic substance derived from the urine of pregnant women has been tried for a wide range of conditions. It is included here because of its usefulness in the treatment of true cryptorchidism. It is of diagnostic

powder.

Action and use. Treatment of cryptorchidism where there are no anatomic lesions causing obstruction of testicular descent.

Dosage. 500 to 1,000 international units 2 to 3 times weekly. Long-continued injection may be dangerous. Should not be maintained after 8 weeks if there is no progressive descent. Should be discontinued if there are signs of precocious puberty.

Dosage forms. *Ampuls* containing varying amounts of powdered preparation of chorionic gonadotropin, brought into solution with the accompanying diluent. The usual sizes are 100 I. U. and 500 I. U. in 2 cc. ampuls; 2,500 I. U in 5 cc.; 1,000, 5,000, 10,000 I. U. in 10 cc The number of I. U. stated means the total in each vial. The diluent supplied usually is sterile distilled water with a preservative. The solution varies as to stability and therefore should be refrigerated and used as soon as possible.

TESTES

Testosterone, the testicular hormone, has been effective as replacement therapy for eunuchoid and castrate males, and in the treatment of hypogonadal states. It has also been used in females in certain cases of metropathia hemorrhagica, menorrhagia, dysmenorrhea, breast engorgement, and for inhibition of the lactogenic hormone, resulting in suppression of lactation.

Side effects: May inhibit spermatogenesis; hypercalcemia, edema may occur; hirsutism; hoarseness; increased libido; enlargement of the clitoris; acne.

METHYLTESTOSTERONE, U. S. P. White powder; odorless, stable in air; affected by light. Insoluble in water; sparingly soluble in vegetable oils.

Actions and uses. Methyltestosterone is used orally for the conditions stated above.

Dosage. Varies with condition. Initial therapy usually 30 to 50 mg. daily in divided doses. Suppression of lactation or breast engorgement, 25 to 30 mg. every 4 hours or 3 times daily for 5 or 6 doses at beginning of lactation (third or fourth day postpartum).

Dosage forms. Tablets, U. S. P., 10 mg., 20 mg., 25 mg.

TESTOSTERONE PROPIONATE, U. S. P. Propionic acid ester of testosterone. White powder; odorless; stable in air. Insoluble in water; soluble in vegetable oils.

Actions and uses. See opening statement above.

Dosage. 10 to 50 mg., intramuscularly 2 to 6 times weekly, according to response. To *induce pubescence* in eunuchoidism, 25 mg. 3 times weekly for several weeks. Maintenance dose according to effect. *Menorrhagia*—10 mg. 3 times weekly before onset of menses. *Metrorrhagia*—25 mg. on alternate days for total monthly dosage not to exceed 150 mg. *Suppression of lactation or breast engorgement*—50 to 75 mg. over period of 2 or 3 days, starting third or fourth day postpartum. (If considerable amounts, ranging from 350 mg. to 400 mg. per month, are given, induction of virilism has been reported in women.)

Dosage forms. Testosterone Propionate *Injection*, U. S. P., *ampuls*, 5 mg., 10 mg., 25 mg., 50 mg. per cc. in oil, in various sizes.

THYROID, U. S. P. Yellowish to buff colored powder; characteristic meatlike odor, saline taste. Contains 0.17% to 0.23% iodine in thyroid combination only (no inorganic or other form of iodine).

Actions and uses. Thyroid, or specifically the thyroid hormone, thyroxin, is used mainly to restore oxygen metabolism to normal, in the presence of a thyroid deficiency state. The hormone appears to be utilized completely since none is excreted.

Prominent effects are increases in oxygen metabolism, pulse rate, nervous irritability. A concomitant and not necessarily desirable effect is weight loss. Onset of action about 1 day after administration. Peak effect about the tenth day and recedes slowly. Continued administration therefore leads to cumulative effects.

Each 12 mg. thyroid (0.1 mg. thyroxin) will raise basal metabolic rate about 2%.

Toxicity. Gross overdosage reproduces the clinical picture of thyrotoxicosis.

Dosage. Should be adjusted to individual need. The U. S. P. usual dose is 30 mg.

Dosage forms. Thyroid *Tablets*, U. S. P.: 15 mg., 30 mg., 60 mg., 120 mg. (each 12 mg. thyroid contains about 0.1 mg. thyroxin).

Chapter 17.

AGENTS USED IN METABOLIC DISORDERS

This section deals with substances which have a special metabolic effect by direct action (e. g. propylthiouracil) or which render an effect by being metabolized (e. g. amino acids, dextrose, etc.).

AMINO ACID AND PROTEIN PREPARATIONS

The object of therapy with protein preparations is to offset protein depletion caused by serious illness (extensive burns, wounds, etc.) It is of special importance for patients unable to satisfy requirements particularly for the amino acids which cannot be synthesized by the body and the usual source of which is in protein foodstuffs taken in the diet. These so-called "essential amino acids" are: lysine, tryptophane, histidine, phenylalanine, leucine, isoleucine, threonine, methionine, valine, arginine.

The administration of protein in readily assimilable form (mainly as constituent amino acids) is accomplished by the use of proteins hydrolyzed through the stages of proteoses, peptones, peptides, and finally, amino acids. These hydrolyzed proteins are known as protein hydrolysates, usually obtained by acid hydrolysis of proteins, but also obtainable in less complete form by enzymatic hydrolysis. They should be used only when it is impossible or not feasible for the patient to take protein in the usual diet.

The minimum requirement (Council on Pharmacy and Chemistry, A. M. A.) for protein hydrolysates is that at least 50% of the total nitrogen present be in the form of alpha amino nitrogen (the remainder usually combined as peptides). This ratio of alpha amino to total nitrogen indicates the degree of hydrolysis. For example, complete hydrolysis of casein gives a ratio of 75%. The 50% minimum provides for nonantigenicity of parenteral forms and minimal allergenic effect of oral forms.

Contraindications. Intravenous use contraindicated in acidosis. Untoward effects—nausea, vomiting, hyperpyrexia, vasodilatation, abdominal pain, convulsions, edema at site of injection, phlebitis, thrombosis.

Dosage. Based on recommended daily intake of total dietary protein of 1 Gm. (approximately 0.14 Gm. nitrogen) per kilogram body weight. Products low in sodium content should be chosen where sodium restriction is advisable.

Dosage forms. For parenteral use, the usual concentrations are 5% of protein hydrolysate, and 5% protein hydrolysate with 5% dextrose. Various powder mixtures are obtainable for oral use. (See also "Parenteral Fluids", p. 110.)

ANTITHYROID DRUGS

PROPYLTHIOURACIL, U. S. P. (6-Propyl-2-thiouracil). White powder; bitter taste. Very slightly soluble in water; sparingly soluble in alcohol.

Actions and uses. Inhibits thyroxin formation by the thyroid. Used in treatment of hyperthyroidism, thyrotoxicosis, thyroiditis, and in the preparation of

must first be utilized.

Propylthiouracil, in contrast to iodine therapy, is more prolonged and constant in effect. In mild and juvenile types of hyperthyroidism, iodine therapy should be tried first.

Toxicity. The adverse reactions are unpredictable. Granulocytopenia, leukopenia, drug fever, dermatitis have occurred.

Dosage. Severe hyperthyroidism: initially, 50 mg. every 8 hours; in milder cases, 50 mg. twice daily. Iodine (approximately 0.3 Gm. potassium iodide daily) should be administered for 2 or 3 weeks prior to thyroidectomy. Effective dose of propylthiouracil is continued until condition is brought under control. Maintenance dose is gauged by the clinical condition of the patient, and by the basal metabolic rate. Patients should be instructed to cease medication and report to physician if any adverse symptoms (sore throat, fever, coryza or malaise) are experienced.

Dosage forms. Propylthiouracil *Tablets*, U. S. P., 50 mg.

CALCIUM COMPOUNDS

Calcium is used to overcome various manifestations of calcium deficiency. Calcium salts are specific in the treatment of hypocalcemic tetany, parathyroid tetany; they are used supplementary to dietary calcium to provide for additional requirements of pregnant and lactating women.

The daily requirement for calcium intake in adults is approximately 0.5 Gm.; for children, 0.9 Gm. to 1.2 Gm. One quart of milk furnishes approximately 1.2 Gm. of calcium and 0.9 Gm. of phosphorus.

Due to liberal oxalate in the average diet, calcium should be administered preferably in the interdigestive period, 1 to 1½ hours after meals. Injection of calcium into the tissues should be avoided.

The calcium compound selected for parenteral use is calcium gluconate. It is also suitable for oral use. Dicalcium phosphate has also been selected for oral use because of the combined calcium and phosphorus content, particularly advantageous for pregnant and lactating women.

CALCIUM GLUCONATE, U. S. P. White, odorless, tasteless powder. Stable in air. One gram slowly soluble in 30 cc. water. Calcium content is 9%.

Actions and uses. See introductory material above.

Dosage. Severe hypocalcemic tetany—5 to 20 cc. of 10% calcium gluconate solution slowly intravenously. Orally, 5 Gm. 3 times daily 1 to 1½ hours after meals, suitable for mild or latent hypocalcemic tetany.

Dosage forms.

Calcium Gluconate *Injection*, U. S. P., *ampuls*, 10 cc., 10%.

Calcium Gluconate *Tablets*, U. S. P., 1 Gm.

DIBASIC CALCIUM PHOSPHATE, U. S. P. (Dicalcium phosphate) $CaHPO_4 \cdot 2H_2O$. White, odorless, tasteless powder. Stable in air. Almost insoluble in water. Calcium content, 23%; phosphorus content, 18%.

Actions and uses. See introductory material above.

Dosage. 6 Gm. daily.

Dosage forms. *Tablets*, 0.5 Gm. *Capsules*, Dibasic Calcium Phosphate (0.5 Gm.) with Vitamin D (330 units), intended particularly for pregnant and lactating [illegible] as 3 times daily between meals.

glucose which is a mixture of [illegible] plete hydrolysis of starch.) White, odorless, sweet powder. One gram soluble in 1 cc. water; in about 60 cc. alcohol.

Actions and uses. Each gram provides 4 calories. Used as nutrient; for supplying fluid; restore blood volume temporarily. Five percent solution is approximately isotonic. (See also chapter on "Parenteral Fluids".) Also effective as a diuretic agent.

Dosage forms. Dextrose *Injection*, U. S. P., available as 5%, 10%, 50% solutions in various size containers.

IODINE (SYSTEMIC USE)

Iodides are used in the prophylaxis of simple endemic goiter and in the management of hyperthyroidism prior to thyroidectomy. This is assumed to increase the iodine content of the thyroid colloid, with a resulting involution of hyperplasia.

The use of Strong Iodine Solution ("Lugol's Solution") has no advantage over the iodides of potassium or sodium, is more disagreeable and irritating, and lacks stability. For these reasons, potassium iodide is recommended for systemic iodine therapy.

POTASSIUM IODIDE, U. S. P. White crystals or powder. Soluble 1:0.7 in water; 1:22 in alcohol; 1:2 in glycerin.

Actions and uses. In thyrotoxicosis, for temporary control of symptoms prior to thyroidectomy.

Toxicity. Appearance of chronic iodine poisoning (iodism) is unpredictable, varying according to the individual. Toxic effects are irritative—mouth, throat, and gum irritation and soreness; increased salivation; sneezing, lacrimation often with inflamed eyelids; skin rash. Rarely fatal; subsides after discontinuance of drug.

Dosage. Prior to thyroidectomy, 0.3 Gm. daily, freely diluted with water or milk.

Dosage forms.

Tablets, N. F. 0.3 Gm.

Potassium Iodide *Solution*, N. F. ("Saturated Solution Potassium Iodide"), containing 1 Gm. per cc.

Chapter 18.

OXYTOCICS

Oxytocic drugs induce or strengthen uterine contraction, by direct smooth muscle stimulation. Their chief use is post partum, to contract the empty uterus and arrest bleeding.

Certain ergot alkaloids and posterior pituitary are the principal oxytocic agents. Of the ergot alkaloids, ergonovine has been selected as having optimal effect. Compared to ergotamine and ergotoxine, it is the least toxic. Ergotamine tartrate has been selected and included in this section for its usefulness in the management of migraine rather than for its oxytocic action.

The posterior pituitary provides the combined actions of an oxytocic factor and of a vasopressor-antidiuretic factor. For oxytocic effect, oxytocin, a product predominantly oxytocic in action (less than 5% has vasopressor effect) has been selected rather than the whole posterior pituitary. Oxytocin, U. S. P. is marketed as "Pitocin." (Posterior pituitary and its vasopressor portion, vasopressin, are further discussed under "Hormones and Synthetic Substitutes" and under "Antidiuretics".)

Some believe that ergonovine is sufficiently rapid in onset and sustained in action to replace posterior pituitary or its oxytocic fraction which, before the advent of ergonovine, were the drugs of choice where rapid effect was desired.

ERGONOVINE MALEATE, U. S. P. White, or faintly yellow, odorless powder; affected by light. Soluble in water, 1:36, in alcohol, 1:120.

Actions and uses. Decidedly more powerful in its effects on the uterus than are the other alkaloids of ergot. This difference is more marked on the puerperal than on the nongravid uterus. The uterine action is the only appreciable effect of moderate doses of ergonovine, unpleasant side reactions being rarely encountered clinically. A slight increase in blood pressure may be encountered. Prolonged therapy or overdosage should be avoided (ergotism).

Dosage. 0.2 mg. (1 cc.) either intramuscularly or intravenously after third stage of labor is completed. Orally, 0.2 mg. every 4 hours for 6 to 12 doses during the puerperium.

Dosage forms.

Ergonovine Maleate *Injection*, U. S. P.; *ampuls*, 0.2 mg. in 1 cc.
Ergonovine Maleate *Tablets*, U. S. P., 0.2 mg.

OXYTOCIN INJECTION, U. S. P.[1] Sterile, aqueous solution of water-soluble oxytocic principle from posterior lobe of the pituitary body of healthy, domesticated animals used for food by man. Each cc. has oxytocic activity of 10 U. S. P. Posterior Pituitary Units. Has less than 5% (less than ½ unit per cc.) of pressor activity.

[1] Oxytocin, U. S. P. has been marketed under the trade name "Pitocin."

indicated if pelvis is contracted or cervix incompletely dilated. *It should not be given intravenously.*

Dosage. 1 cc. intramuscularly to cause immediate post partum contraction of uterus. If given before delivery, small doses are used (0.06 cc. to 0.2 cc.), repeated if necessary, in 20 to 30 minutes.

Dosage form. Pitocin (Oxytocin *Injection*, U. S. P.) *ampuls*, 0.5 cc. and 1 cc.

As previously explained, Ergotamine Tartrate, U. S. P., is described here for its use in the management of migraine rather than for its oxytocic effect:

ERGOTAMINE TARTRATE, U. S. P.[3] Colorless powder usually containing solvent of crystallization. Soluble in water, 1:500; in alcohol, 1:500.

Actions and uses. Stimulates smooth muscle (oxytocic effect). Has been used to relieve pain of migraine and shorten attacks; prophylactic use is not advised. Prolonged therapy or overdosage may cause toxic effects (ergotism). Gangrene has been reported after continued use over a period of "some days".

Dosage. 0.25 mg. subcutaneously followed in 2 or 3 hours by 0.5 mg. if no untoward effects or if initial dose ineffective. May be given orally, 2 or 3 tablets (1 mg.) hourly sublingually or swallowed, up to 8 or 9 mg. Oral use not as effective as subcutaneous.

Dosage forms.

Ergotamine Tartrate *Injection*, U. S. P., *ampuls*, 0.5 cc. (0.25 mg.) and 1 cc. (0.5 mg.).

Ergotamine Tartrate *Tablets*, U. S. P., 1 mg.

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[3] Ergotamine Tartrate, U. S. P. has been marketed under the trade name "Gynergen."

The cholinergic division of the autonomic nervous system is generally antagonistic to the adrenergic (orthosympathetic) division. Parasympathomimetic drugs act mainly by inhibiting cholinesterase activity, or by direct acetylcholine-like effect. Thus pilocarpine, physostigmine, etc., elicit the following responses: bradycardia, miosis, contraction of bronchial, intestinal, and uterine muscles, and increases in glandular activities. Atropine opposes these effects through interference with the action of acetylcholine.

The drugs used fall into three classes: (1) Choline esters, acting directly; (2) Cholinesterase inhibitors; (3) Alkaloids having direct effect on receptor mechanism.

CHOLINE ESTERS

CARBACHOL, U. S. P. White or faintly yellow crystals or powder; odorless hygroscopic. Soluble in water, 1:1; alcohol, 1:50.

Actions and uses. Same pharmacologic effects as acetylcholine. In contrast to other esters, it has a lessened cardiac action and a powerful miotic effect. Useful for reduction of intraocular tension in glaucoma simplex. Other drugs of this series are more effective for other parasympathetic actions.

Dosage. Glaucoma simplex—one drop of 1.5% solution instilled at intervals of 8 to 12 hours. May also be used as 1.5% ointment.

METHACHOLINE CHLORIDE, U. S. P. (Acetyl-beta-methylcholine chloride) (Mecholyl Chloride). Colorless or white crystals or powder. Very soluble in water and freely soluble in alcohol; very deliquescent.

Actions and uses. This drug is closely related to the parasympathetic neurohormone, acetylcholine. Its actions are similar, but less evanescent. It causes *powerful stimulation of the cholinergic system, especially slowing the heart,* lowering the blood pressure, dilating blood vessels, and increasing gastrointestinal peristalsis. It is used to correct paroxysmal tachycardia.

Toxicity. Should not be used on patients with asthma, or coronary artery disease. Antidote: atropine.

Dosage. 10 to 25 mg. subcutaneously. Never use intravenously.

Dosage forms. *Ampuls,* 25 mg. (to be dissolved in sterile distilled water).

CHOLINESTERASE INHIBITORS

PHYSOSTIGMINE SALICYLATE, U. S. P. (Eserine salicylate.) White or faintly yellow crystals or powder. Acquires red tint on long exposure to light and air. Soluble in water, 1:75; alcohol, 1:16.

Actions and uses. Produces cholinergic effect by *inhibiting cholinesterase.* *Eye:* Used in treatment of glaucoma. As a miotic to break adhesions of iris and lens, alternating with atropine. Used after a mydriatic, where necessary, to return pupil to normal size thus reducing danger of increased intraocular pressure. Preferable to pilocarpine after cataract extraction.

Intestine. To restore bowel activity in cases of gastrointestinal atony (paralytic ileus following anesthesia; distention following certain acute infections and toxic processes).

striction. Antidote: 0.5 mg. to 2 mg. atropine intramuscularly or intravenously, depending on degree of toxicity.

Dosage.

Glaucoma—0.1% to 1% solution.

Promote peristalsis—2 mg. intramuscularly.

Dosage forms. *Powder* for solution; hypodermic *tablet*, 1 mg., 1.2 mg., 1.5 mg.

NEOSTIGMINE BROMIDE, U. S. P. (Prostigmine Bromide). White, crystalline powder. Odorless, bitter taste. Soluble in water, 1:1; soluble in alcohol.

Actions and uses. Action similar to physostigmine. Used *orally* for treatment of myasthenia gravis.

Toxicity. Same as for physostigmine.

Dosage. 15 mg. 3 times daily; may be cautiously increased, if necessary, to 30 mg. 3 times daily.

Dosage form. *Tablets*, 15 mg.

NEOSTIGMINE METHYLSULFATE, U. S. P. (Prostigmine Methylsulfate). White, crystalline powder. Odorless, bitter taste. Soluble in water, 1:10; less soluble in alcohol.

Actions and uses. Action similar to physostigmine. Used for prevention and treatment of postoperative intestinal paresis, and bladder paresis.

Dosage. Prevention of postoperative distention—1 cc. of 1:4,000 solution subcutaneously or intramuscularly every 4 to 6 hours, starting 24 hours preoperatively and continued until second or third postoperative day.

Treatment of distention—1 cc. of 1:2,000 solution subcutaneously or intramuscularly.

Myasthenia gravis—1 cc. of 1:2,000 initially; subsequent doses depend on response to initial dose.

Dosage forms. *Ampul:*

1 cc., 1:4,000 (0.25 mg.).

1 cc., 1:2,000 (0.5 mg.).

DIRECT RECEPTOR EFFECT

PILOCARPINE HYDROCHLORIDE, U. S. P. Colorless, translucent, odorless, faintly bitter crystals. Hygroscopic and affected by light. Soluble in water, 1:0.3; alcohol, 1:3.

Actions and uses. Central effects unimportant. Used as a miotic and as a diaphoretic.

Eye.—Produces miosis and spasm of accommodation by peripheral stimulation of oculomotor nerve. Miosis begins in 15 minutes (independent of concentration), reaches maximum in 30 to 60 minutes and disappears in 24 hours. Spasm of accommodation also begins in 15 minutes and lasts about 2½ hours. Intraocular tension first increased, then more persistent fall. *Dosage:* ¼% to 4%, usually 1% to 2% used as milder substitute for physostigmine in glaucoma. Ointment, 1%, often used at bedtime.

Diaphoresis. Used in nephritis, to relieve kidney and decrease the edema. ***Usual dose,*** 5 mg. subcutaneously. Antidote: Atropine.

Dosage form. *Powder; ointment, ophthalmic,* 1%; *tablets, hypodermic,* 5 mg.

Chapter 20.

PARENTERAL FLUIDS

This group of parenteral fluids includes only the fluids given in relatively large quantities for the purpose of general supportive treatment, including maintenance of positive nitrogen balance and correction of fluid and electrolyte balance. They are used chiefly for treatment (replacement, supportive) in conditions in which the body is unable to maintain itself, as in shock, severe burns, pre- and post-operative care, and in certain metabolic disorders.

In general, to maintain an individual on complete parenteral feedings over a short period (less than 5 days) without complications induced by electrolyte imbalance, one may use the following general formula which is a good base in almost any case:

3,000 cc. fluid total:

1,000 cc. 5% dextrose in isotonic sodium chloride solution.

1,000 cc. protein hydrolysate.

1,000 cc. 10% dextrose in distilled water.

Administration. Preferable method is intravenously but on occasion isotonic solutions may be given by hypodermoclysis.

Contraindications. In general the protein and amino acid preparations, and human plasma give the most difficulty, with reactions of hyperpyresis, nausea or vomiting, abdominal cramps.

Classification of the solutions used for general supportive therapy may be made into the following five groups:

(1) CARBOHYDRATE SOLUTIONS: furnish calories at the rate of 4 calories per gram of carbohydrate.

5% dextrose in distilled water. (Solution is isotonic.)

10% dextrose in distilled water—where needs of patient demand more calories with limited fluid.

(2) SALINE SOLUTIONS: furnish acid, base, or a balanced electrolyte fluid. The apparent function of sodium, the cation of the extracellular fluid, is osmotic. Change in sodium concentration creates serious upset in fluid distribution. Dehydration causes sodium chloride depletion which is more serious than the water loss. This calls for administration of sodium chloride. Heat cramps and shock are forms of sodium depletion observed clinically. Heat cramps occurring in persons who perspire copiously and who are engaged in hard labor, may be prevented by taking sodium chloride tablets (1 Gm., enteric coated) with drinking water.

For **sodium depletion** brought about by **shock**, where *parenteral administration is not necessary*, and where patient *can take fluid by mouth*, a solution of one teaspoonful sodium chloride and two-thirds teaspoonful of sodium bicarbonate in a quart of water, has been found effective.

in 20 cc.).

Use. Intravenously, for correction of potassium deficienc
acidosis, excessive vomiting from intestinal obstruction, sys
severe burns, pyloric stenosis, infantile diarrhea, hyperventila
urinary obstruction, adrenocortical insufficiency.

Dosage. 20 cc. of 40 milliequivalent solution (2.98 Gm.)
1,000 cc. with isotonic sodium chloride solution or dextrose,
water, gives a solution providing 40 milliequivalents in potassi
ride ions.

(3) PROTEIN PREPARATIONS: See "Agents Used in Metab
PROTEIN HYDROLYSATE, 5%.
PROTEIN HYDROLYSATE, 5%, WITH DEXTROSE, 5

(4) COMBINATIONS OF THE ABOVE:
5% DEXTROSE IN ISOTONIC SODIUM CHLORIDE

(5) HUMAN PRODUCT SOLUTIONS:
WHOLE BLOOD.

NORMAL HUMAN SERUM ALBUMIN, U. S. P.: for
demonstrated hypoalbuminemia (cirrhosis and nephrotic

Dosage of the above two products depends on individual ne
of Normal Human Serum Albumin, an average dose is 2.2 cc. per
at rate of no more than 2 cc. per minute; usually with isotonic
solution or with 5% dextrose in water.

SPECIAL PURPOSE SOLUTIONS

Alkali Therapy:

SODIUM LACTATE INJECTION, U. S. P., ⅙ MOLAR. I
lactate is used. The dextrarotatory portion is converted into live
the levorotatory form is oxidized to bicarbonate. 1 l. equivalent
effect to 340 cc. of 5% sodium bicarbonate, and to 1 l. of 3% de
ketogenic effect. Conversion to bicarbonate occurs in 1 to 2 hours

SODIUM BICARBONATE SOLUTION, 5%, intravenously,
neutralizing effect.

Chapter 21.

SCLEROSING AGENTS

SODIUM MORRHUATE INJECTION, U. S. P. Sterile solution of sodium lts of the fatty acids of cod liver oil.

Actions and uses. Sclerosing agent for the obliteration of varicose veins. *ncentrations greater than 5% are not recommended.* The possibility of sensi- ity or idiosyncrasy to the drug should be kept in mind. A test dose, as described der "Dosage," is used as a precaution.

Dosage. Preliminary test dose of 0.5 to 1 cc. of 5% solution effects of which ould be observed for *24 hours* before further injections. An average of 1 cc., d not more than 2 cc. is injected at any one site. Total injections in one day ries with patient and should not exceed 5 cc. Injections of the saphenous ln at the time of ligation may require 5 to 10 cc.

Due to possible development of sensitivity it is recommended that no more an 5 days elapse between the first two injections.

Dosage forms. *Injection*, U. S. P., *Ampuls*, 5%, 2 cc., 5 cc., 25 cc.

In the event of sensitivity to sodium morrhuate, dextrose solutions may be ed.

DEXTROSE INJECTION, U. S. P. *Injection*, U. S. P., *Ampuls*, containing % of dextrose are used.

Dosage. 5 to 20 cc. of 50% solution depending on size of vein.

Dosage forms. *Injection*, U. S. P., *Ampuls*, 50%, 50 cc.

Chapter 22.

SEDATIVES AND HYPNOTICS

BARBITURIC ACID DERIVATIVES

The series of hypnotic drugs derived from barbituric acid are acid to litmus, sparingly soluble in water and soluble in alcohol. They may be made water-soluble by conversion to salts (usually the sodium salt). The salts are unstable in solution, decomposing with the formation of ammonia and other products; in acid media, the barbiturate is precipitated from the salt.

With barbituric acid (malonylurea) as the primary radical, the various derivatives are formed by replacing both hydrogens of the acid by alkyl (e. g., ethyl, allyl) or aryl (e. g., phenyl, cyclohexenyl) groups. Thus, phenobarbital is phenylethyl barbituric acid. The nature of these substituted radicals determines the potency, duration of action, and metabolic fate of compounds formed.

Pharmacologic Action of the Group

Major action is cerebral depression. Barbiturates are used chiefly as hypnotics. Adequate oral doses produce sleep in 20 to 60 minutes. They are not analgetics per se, but reduce reaction to pain. They also act as anticonvulsants, anesthetics, and spasmolytics.

Barbital and phenobarbital are excreted in the urine. Pentobarbital and secobarbital (seconal) are destroyed in the body chiefly in the liver. Thiobarbiturates probably are destroyed in the liver and other tissues.

Side actions. The barbiturates depress cortical functions. Hence, individual responses are not always predictable. Thus, if a particular barbiturate releases undue excitement in one patient and not in another, it may be the patient and not the drug.

Addiction. Definite tolerance, habituation, and physical dependence result from prolonged abuse of barbiturates. Prominent withdrawal phenomena are restlessness, irritability, hyposomnia, convulsions, and psychosis.

Barbiturate poisoning. Lavage freely with 10% sodium bicarbonate solution; or give emetic (15 Gm. sodium sulfate) if patient is not comatose.

If in coma, 200 cc. of 25% dextrose intravenously; 10 to 40 mg. (1 to 4 cc. of 1% sol.) of amphetamine sulfate intramuscularly, followed by 10 to 20 mg. (1 to 2 cc.) every half hour, not to exceed total of 400 mg. (40 cc.). One cc. per minute of 1:1,000 picrotoxin solution until corneal reflexes reappear has also been used, but requires close expert supervision and great caution. Carbon dioxide, 5%, and oxygen, 95%, or oxygen alone for hypoxia. Airway if necessary. If blood pressure is low, give 10 mg. amphetamine sulfate orally, or 25 mg. ephedrine sulfate subcutaneously.

Numerous barbituric acid compounds have been introduced. There is little clinical need for more than one drug having long duration of action, one of intermediate, one of short, and one of ultra-short action. The three U. S. P. drugs and one N. N. R. drug selected should be adequate for these needs.

U. S. P. usual dose. 30 mg. *Sedative use:* 15 mg. to 30 mg. 3 times a day. *Infants,* birth to 18 months, 4 mg. to 8 mg.; *children,* 18 months to 12 *years,* 15 mg. Sedation occurs within 1 to 2 hours; sedative dose is ⅓ to ¼ the hypnotic dose. For sedation in anxiety tension states, hyperthyroidism, essential hypertension, nausea or vomiting of functional origin, seasickness, acute labyrinthitis, pylorospasm in infants, chorea, cardiac failure, whooping cough, etc.

Hypnotic use: Not recommended, because onset is slow and duration of action is too long. *Control of epilepsy:* Dose must be carefully regulated for best effect. Sometimes used alone and sometimes in combination with other anticonvulsants. When used alone, average dose, 0.1 Gm. to 0.15 Gm. daily; in *divided doses;* or in one dose before retiring, if nocturnal epilepsy; or in morning for diurnal epilepsy.

Dosage forms.

Tablets, U. S. P. 15 mg., 30 mg., 0.1 Gm.

Tablets, U. S. P., *hypodermic,* 60 mg.

Phenobarbital Elixir, U. S. P. containing 15 mg. per 4cc.

Ampuls (phenobarbital sodium), 0.12 Gm. of powder (Sterile Phenobarbital Sodium, U. S. P.) or solution in propylene glycol (Phenobarbital Sodium Injection, U. S. P.).

Intermediate Duration

PENTOBARBITAL SODIUM, U. S. P. (Ethyl-1-methylbutyl barbituric acid, sodium salt). ***U. S. P. usual dose:*** 0.1 Gm. *Sedative dose:* 50 mg. *Hypnotic dose:* 0.1 Gm. Total action, 6 to 10 hours. In maniacal conditions, 0.25 to 0.5 Gm., by vein if necessary. *Anticonvulsant dose:* 0.25 Gm. to 0.5 Gm. by slow intravenous injection (traumatic tetanus, strychnine poisoning, meningitis, chorea, status epilepticus, tetany, eclampsia, cocaine or procaine poisoning). *For basal anesthesia:* 0.1 Gm. evening preceding operation, and a second dose of 0.1 Gm. to 0.2 Gm. 2 hours preoperatively, and repeated 1 hour preoperatively

Dosage forms.

Capsules, U. S. P. 50 mg., 0.1 Gm.

Suppositories, 0.12 Gm.

Ampuls, 0.25 Gm. powder (Sterile Pentobarbital Sodium, U. S. P.).

Short Action

SECOBARBITAL SODIUM, N. N. R. (Seconal Sodium). (Allyl 1-methylbutyl barbituric acid, sodium salt).

Average hypnotic dose. 0.1 Gm. to 0.2 Gm. Action usually shorter than with pentobarbital. Smaller doses (50 mg.) are sedative. *Preanesthetic sedative:* 0.2 Gm. to 0.3 Gm. ½ to 1 hour before going to surgery. *In obstetrics:* Initial dose of 0.3 Gm. followed by 0.1 Gm. to 0.2 Gm. doses at intervals up to total of no more than 1.2 Gm. in 12-hour period.

Dosage forms.

Seconal Sodium *Capsules,* 50 mg., 0.1 Gm.

Seconal Sodium *Suppositories:* 0.12 Gm., 0.2 Gm.

Seconal Sodium *Ampuls,* 0.25 Gm., powder, to be dissolved in 5 cc. of dist. water to make 5% solution.

DIPHENYLHYDANTOIN SODIUM, U. S. P. White odorless powder; freely soluble in water, hydrolysing readily; bitter taste.

Action. Diphenylhydantoin sodium is chemically and pharmacologically related to the barbituric acid derivatives. It differs from the barbiturates mainly in its weaker hypnotic action and its more effective action in controlling seizures of epilepsy, especially the grand mal type.

Toxicity. The drug has shown varying side effects in most patients, generally between the third and tenth day of treatment. The chief side actions are vertigo, dry skin, ataxia, fever, nausea, vomiting, blurred vision, pruritus, feeling of insitude, ptosis, dyspnea and dysphagia, mental confusion. Continued use often causes gum hyperplasia. The strong alkalinity of the drug may cause gastric distress which may be diminished or avoided by giving the drug after meals with half a glass of water.

Dosage. *U. S. P. usual dose*, 0.1 Gm., for adults, three or four times daily before meals, according to individual need. The dose may be increased up to 0.2 Gm. three times daily. If gastric distress occurs, give after meals with one-half glass of water. *Children under 6 years:* 30 mg. mixed with syrup or suitable flavor disguise, twice a day before meals. If necessary, increase. *Children over 6 years:* 60 mg. three times a day before meals for 1 week; if necessary, then gradually increase to minimum dose needed to control effects. Give with at least one-half glass of water to combat gastric irritation.

Dosage forms. *Capsules*, U. S. P., 30 mg.; 0.1 Gm.

TRIMETHADIONE, U. S. P. (Tridione). White, granular, crystalline substance with slight camphorlike odor; soluble in water, freely soluble in alcohol.

Action and uses. Anticonvulsant, used in epilepsy, particularly for *true* petit mal seizures. It is ineffective in grand mal. It may be useful in psychomotor (diencephalic) epilepsy, especially when diphenylhydantoin sodium alone is not effective. It may also be used with phenobarbital (or diphenylhydantoin) in mixed epilepsy, properly adjusted to control both the petit mal and grand mal attacks.

Toxicity. Adverse reactions are said to be infrequent. If present, they occur as gastric irritation, nausea, skin eruptions, photosensitivity, blurring of vision. Photophobia said to be less frequent in children than in adults. Repeated complete blood studies should be made, since aplastic anemia with depression of all elements of peripheral blood has been reported. Because of this, patients should be carefully supervised. Contraindicated in advanced renal or hepatic disease, or disease of the optic nerve, or any type of blood dyscrasia.

Dosage. In petit mal, 1 to 2 Gm. daily in divided doses of three to seven 0.3 Gm. capsules. *Children under 6 years:* Begin with 0.15 Gm. to 0.3 Gm. three times daily, increasing if necessary. Tablets of the drug contain appreciable amounts of magnesium trisilicate as an absorbent and such tablets are contraindicated in large quantities for children on a ketogenic diet.

Dosage forms.

Tridione *Capsules*, 0.3 Gm.
Tridione *Tablets (coated)* 0.15 Gm.
Tridione *Solution*, 0.15 Gm. per 4 cc.

WHISKY, N. F. Alcoholic liquid prepared from the fermented mash of malted cereal grains; alcoholic content between 47% and 53% by volume.

Action. Its action, due to its alcohol content, is that of central nervous system depressant (hypnotic dose, 90 to 120 cc.); release of inhibitions gives impression of stimulation. Small doses (30 to 45 cc.) cause vasodilatation and increased blood flow, helpful in coronary artery and in peripheral vascular disease, and have been said to stimulate respiration reflexly but such effect is little and uncertain. With egg and milk, useful for caloric content and for relaxing effect in convalescent or febrile patients.

Contraindications. Hepatic, renal disease, gastrointestinal ulcer, epilepsy.

ALDEHYDE DERIVATIVES

PARALDEHYDE, U. S. P. Colorless liquid having a strong pungent odor and burning taste. Miscible with water (1:8) and freely miscible with alcohol. Should be preserved in well-filled, tight, light resistant containers holding not more than 120 cc. and preferably at a temperature not above 30° C.

Action. Paraldehyde is one of the best of the hypnotics and sedatives, and one of the least toxic. Doses of 4 cc. to 8 cc. produce normal sleep in 10 to 15 minutes. It probably would enjoy wider use if it were not for its pungent odor and unpleasant taste. It is used effectively in patients with delirium tremens, those mentally disturbed, and those in the convulsions of status epilepticus.

Paraldehyde is destroyed in the body to the extent of 70% to 98%; 11% to 28% is exhaled; 0.1% to 2.5% is excreted in the urine.

Dosage. Usual *U. S. P. dose is* 4 cc. given with cracked ice, ice water, milk, aromatic elixir, tea, wine, or fruit juice. This dose may be given as needed and increased to 10 or 15 cc. if necessary. It may also be given rectally, in isotonic sodium chloride solution or in olive oil.

BROMIDES

Since the bromides offer no advantage over other sedatives and hypnotics and since their use is prone to cause serious intoxication of an insidious nature, they have not been included among the sedatives and hypnotics.

Chapter 23.

SERUMS AND VACCINES

Applied Immunity and Immunization Procedures

Definition of Terms

Antiserum—A serum containing specific immune substances.

Antitoxin—An antagonistic substance elaborated by the body and found in the blood after stimulation by a specific toxin.

Carrier—A person who harbors in the secretions from his nose, throat, or elsewhere, the infectious agent of a disease without showing the clinical manifestations of the disease.

Communicable—Applied to any disease in which the causative agent can be transmitted to another person either directly or indirectly.

Contact—A person who has been exposed to a communicable disease.

Contagious—Applied to an infectious disease which is usually transmitted by direct contact.

Immunity—The state of incapability of acquiring a particular infectious disease upon exposure.

a. *Natural immunity:* inherited or congenital resistance.

b. *Acquired, active immunity:* from an attack of the disease.

c. *Acquired, active, induced immunity:* from the injection or ingestion of an antigen which leads to the production in the body of specific antibodies.

d. *Acquired, passive immunity* (temporary in character): from the injection of antitoxin or other antiserum.

Incubation period—The period between exposure to a disease and the onset of symptoms.

Infection—Invasion of tissues of the body by pathogenic agents until production of injury.

Infectious—Applied to transmissible agent such as a bacterium, a parasite, or a virus.

Inoculation—The introduction of an infectious agent or vaccine into the body.

Isolation—The procedure of keeping a carrier or patient with a contagious disease in a place and under conditions which will prevent the spread of disease.

Quarantine—Restriction of freedom of movement of persons who have been exposed to communicable disease for a period of time equal to the longest usual incubation period of the disease to which they have been exposed.

Serum—See antiserum.

Toxin—A poison elaborated by a micro-organism. Toxins may be injected in small amount to produce acquired antitoxic immunity.

Toxoid—A toxin detoxified by the addition of a chemical, such as formaldehyde, so that it is less likely to cause a reaction when injected, but is still antigenic.

Vaccine—A preparation of an infectious agent or its products which, when injected or ingested, may induce [illegible] against the

Desensitization Procedures

Upon the administration of any kind of serum, all patients regardless of history should be tested for sensitivity to the serum in question. Information should be obtained by questioning if the patient has had asthma, vasomotor rhinitis or is sensitive to horse emanation, or whether horse serum has been used previously.

Skin test. The skin test consists of the intradermal injection of 0.05 cc of serum diluted 1:20 with isotonic sodium chloride solution. A similar injection of saline solution alone is used as a control. A positive test consists of the appearance within 30 minutes of an urticarial wheal with erythema of more than 1 cm. in diameter. If a positive reaction occurs, desensitization of the patient should be attempted.

Ophthalmic test. Material is diluted 1:10 with Isotonic Sodium Chloride Solution, U. S. P. One drop is instilled in conjunctival sac of one eye; the other eye is used as a control, with or without the saline diluent. Reddening in 30 minutes is positive.

Desensitization. The following method of desensitization is recommended: 0.05 cc of a 1:20 dilution of serum subcutaneously. If 15 minutes later no untoward local or systemic symptoms occur the dose may be doubled every 30 minutes until 1 cc. is given. Then 0.1 cc. is given intravenously. The intravenous dose may be doubled every 20 minutes very slowly, until the required amount is given. If the injection is followed by systemic symptoms (edema, urticaria, respiratory distress) the same dose should be repeated at 1-hour intervals. In highly sensitive patients the intravenous route is contraindicated. In persons allergic to horse serum, bovine serum may be used instead. A hypodermic syringe containing 1:1,000 solution of epinephrine hydrochloride should always be at hand while doing test or administering serum, in case reaction occurs.

ANTISERUMS

ANTI-HEMOPHILUS INFLUENZAE TYPE B SERUM (RABBIT), N. N. R. For use in influenzal type B organism—indicated in children below 2 years of age and/or in severe cases of any age. The total dose of serum is inversely proportional to the spinal fluid dextrose:

Spinal Fluid Dextrose	*Dosage in Serum*
Under 15 mg. per 100 cc.	100,000 units.
15-25 mg. per 100 cc.	75,000 units.
25-40 mg. per 100 cc.	50,000 units.
Over 40 mg. per 100 cc.	25,000 units.

The serum is diluted in isotonic sodium chloride solution—10 cc. of solution per kilogram body weight. Slowly administered intravenously. Intramuscular administration is also adequate. The treatment of choice consists in the use of aureomycin alone or combined with sulfonamides.

Dosage form. 25 cc. *ampul* (containing no less than 25,000 provisional units).

ANTIVENIN (CROTALUS). 50 cc. or more intramuscularly or subcutaneously near the snake bite. Used for the bite of all of the Crotalus family (rattlesnake, copperhead, water moccassin). Ampuls, material for 15 cc. solution, with 15 cc. distilled water diluent and 1 cc. (1:10) normal horse serum for sensitivity test.

ANTIVENIN (LATRODECTUS MACTANS), N. N. R. 2.5 cc. solution larly for the bite of black widow spiders. Ampuls, material for 2.5 cc. solution with 2.5 cc. distilled water diluent and 1 cc. (1:10) normal horse serum for sensitivity test.

DIPHTHERIA ANTITOXIN, U. S. P. (equine serum) (500 units per cc.). A preliminary testing of the patient sensitivityto horse serum should always be made before the antitoxin administration: 0.05 cc. of 1:20 dilution of antitoxin is injected into the skin of the anterior surface of the forearm. If after 30 minutes there is no reaction (an unelevated erythema less than 0.5 cm. in diameter on the site of injection read as negative), administration of the antitoxin may proceed. *Treatment:* Must be prompt and adequate. Far less harm will be done by the administration of an occasional unnecessary dose of antitoxin than by delay in the use when required. There is reasonable basis for the use of large doses of serum. In general the average is 100 units of antitoxin per pound body weight in mild cases, and 5 times this amount for the severe form. It should be administered in a single dose, intravenously, except in the very mild case where intramuscular injection is satisfactory.

Dosage forms. *Ampuls,* (treatment), 10,000 units, 20,000 units, 40,000 units.

DIPHTHERIA TOXIN, DIAGNOSTIC, U. S. P. (for Schick Test). The Schick test consists of the intracutaneous injection of 1/50 (MLD) of toxin contained in 0.1 cc. of a proper diluent. Four types of reactions within 24–48 hours are usually observed when test and control are adequately done:

a. *Positive reaction.* Patient is susceptible to diphtheria.

b. *Negative reaction.* Patient is immune to diphtheria.

c. *Pseudo reaction.* Patient is immune to diphtheria but allergic to the protein in test solution.

d. *Positive combined reaction.* Patient is susceptible to diphtheria and also allergic to protein in test solution.

The control test consists of a material identical with that used for the test except that the toxin has been destroyed by heat. In some clinics, the control test is omitted, the reading of the Schick test being made on fifth *day*, when the pseudo-reaction usually has disappeared.

Dosage forms. *Ampuls:* 1 cc. (10 tests); 5 cc. (50 tests); 10 cc. (100 tests).

GAS GANGRENE ANTITOXIN, PENTAVALENT, N. F. (Therapeutic). Each vial of the pentavalent antitoxin contains at least 10,000 units of Cl. perfringens antitoxin, 10,000 units of Cl. septicum antitoxin, 1,500 units Cl. oedematiens (Novyi), 1,500 units Cl. bifermentans (Sordelli) and 3,000 units of Cl. histolyticum antitoxin.

Dosage. An initial dose of 1 to 4 vials, each containing the minimum therapeutic dose, should be administered intravenously or intramuscularly to overcome the toxin. Supplementary intramuscular injections of antitoxin every 4 hours may be advisable, depending on the condition of the patient. Adequate surgical treatment and systemic chemotherapy (sulfonamide, aureomycin, penicillin) are necessary supplements to the antitoxin treatment.

GAS GANGRENE ANTITOXIN FOR PROPHYLAXIS: TETANUS AND GAS GANGRENE ANTITOXINS, N. F. Each vial contains not less than 2,000 units of Cl. perfringens and Cl. septicum each, plus 1,500 units of tetanus antitoxin.

plasma. (160 mg. per cc.)

Indications, dosage and administration:

Measles. For prevention: 0.1 cc. per pound body weight. For modification: 0.02 cc. per pound body weight. For either indication, the globulin should be given within the first 6 days after initial exposure. The usual duration of protection following an effective dose of gamma globulin is about 4 weeks. A modified attack of measles will usually provide an active and permanent immunity.

Rubella. Pregnant women exposed to rubella should be protected with 10 cc. of immune serum globulin. It should be noted that there is a high incidence of congenital anomalies if rubella does develop during the first trimester.

Chicken Pox. The protection offered by gamma globulin is still questionable. The usual dose is 2 cc. on exposure.

Mumps. Immune globulin may protect the patient if given soon after exposure, and might ameliorate the clinical course of the mumps, if given later (see hyperimmune serum).

Scarlet Fever. The use of gamma globulin confers protection for about 35 days. (Only the toxic manifestations due to the erythrogenic toxin.) Penicillin should be used primarily in the treatment of the disease.

Infectious Hepatitis. Any age, upon exposure, 0.1 cc./lb. body weight; repeat in 3 weeks.

Route of Administration. Gamma globulin should be given intramuscularly, preferably in the buttocks. Should not be given intravenously.

Reactions. No systemic reactions have been observed. Occasional local tenderness at the site of injection.

Dosage forms. *Ampuls*, 2 cc., 10 cc.

PERTUSSIS IMMUNE SERUM (HUMAN) (Passive immunization).

Prevention. Particularly useful for young infants exposed to whooping cough. Two doses of 2.5 cc. Antipertussis Serum (Hypertussis), or vacuum dried Pertussis Immune Serum (Human) in amounts stated in the instructions, given intramuscularly, will protect completely 50% of the exposed infants and will modify the disease in the remainder.

Treatment. 3 to 4 doses of 2.5 cc., or vacuum dried hyperimmune serum, in amounts given in the instructions, 3–4 times in 48-hour intervals. Recently the use of aureomycin appears to be effective against pertussis.

Dosage forms. *Ampuls*, 2.5 cc. (concentrated); 20 cc. (vacuum-dried, unmodified with 20 cc. diluent).

RABIES HYPERIMMUNE SERUM (rabbit). Now being investigated experimentally and shows good promise. Used in conjunction with the vaccine.

SCARLET FEVER STREPTOCOCCUS TOXIN, N. F. (Dick Test Toxin). For Dick test: intracutaneous injection of 0.1 cc. Area of redness greater than 1 cm. in diameter in 24 hours is recorded as positive. A positive reaction occurring before the onset of the early course, and changing to negative later on is highly suggestive of scarlet fever. (Active immunization against scarlet fever is not recommended as a public health measure, nor is it of value for the exposed individual. Local and general reactions are severe.)

Dosage. 3,000 to 15,000 units intramuscularly, after preliminary testing for sensitivity to horse serum. (Convalescent serum human (500 units/cc.) in doses of 60–300 cc., or immune serum globulin, 1 cc./lb. up to 60 cc., intramuscularly, might be used if antitoxin is ineffective or contraindicated.)

Blanching test (Schultz-Charlton test). Intradermal injections of 0.2 cc. of convalescent serum or antitoxin into an area where the rash is present; local blanching of the rash in 6 to 12 hours is positive for scarlet fever.

Dosage forms. *Ampuls*, 3,000 units; 9,000 units.

TETANUS ANTITOXIN, U. S. P. Not less than 400 units per cc. of antitoxin. (An "American unit" of antitoxin is 10 times the least amount of serum necessary to save the life of a 350 gm. guinea pig for 96 hours against the standard test dose of toxin. It is approximately double the strength of the "International Unit.")

Dosage, prophylactic (passive immunization). The generally recommended dose of antitoxin is 1,500 to 3,000 units injected subcutaneously after a preliminary skin test for sensitivity to the serum.

Dosage for active infection: 40,000 to 80,000 units should be injected after an infiltration of the areas around the wound with 5,000 to 10,000 units; the rest may be divided into intramuscular and intravenous injections. (See tetanus toxoid for active immunizations.)

Dosage forms. *Ampul*, 1,500 units (prophylactic); 10,000, 20,000 units (therapeutic).

VACCINES

Vaccines and *toxoids* are prepared from living attenuated or killed antigenic agents which when injected into the body cause an active immunization by the body against this particular agent without the presence of clinical disease. The advantages in the use of vaccines over the serums are:

1. No foreign protein is given, hence fewer reactions.
2. On subsequent exposure to antigen, body response against it is greater.

The disadvantage is that a much longer time is required for this method of immunization.

CHOLERA VACCINE, N. F. Sterile suspension of killed *cholera vibrios* with a high antigenic efficiency, in a suitable diluent. Each cc. contains at least 8,000 million cholera organisms, preserved with phenol. It is used for the prevention of cholera and administered in two or three doses. The first dose is 0.5 cc., the second dose is 1 cc., subcutaneously. 7 to 10 days later, a third dose of 1 cc. is advisable. A stimulating dose of 1 cc. every 6 months while danger of infection exists has been suggested. Children under 4 years of age should receive 3 doses of 0.25 cc. each. Children over 4 years the same dosage as adults.

Dosage form. *Ampuls*, 20 cc. (8,000 million per cc.).

MUMPS VACCINE. Prepared from the allantoic fluid of the infected chick embryo.

Indications. Immunization against mumps. Not recommended in children below 13 years of age.

Dosage. 2 injections of 1.0 cc. each administered subcutaneously or intramuscular at an interval of 1 to 4 weeks between injections. Annual booster necessary to keep the antibody titer at an adequate level. Contraindicated in

against the disease and its complications. Immunity produced on recovery from mumps is manifested by a positive skin test.

Dosage. 0.1 cc. intradermally into the inner surface of the forearm. The test should be read in 24 to 36 hours.

PERTUSSIS VACCINE, U. S. P. (Pertussis Vaccine, Fluid) (At least 10,000 million H. pertussis phase I per cc.) Basic immunization at 4 to 12 months of age.

Dosage. Three 0.5 cc. doses at intervals of 3 to 4 weeks for total dose of 50,000-80,000 million. (See Immunization Schedule, p. 130, for booster dose.)

Dosage form. *Ampuls:*

20,000 million per cc. (5 cc., 12.5 cc., 20 cc., 50 cc.)

40,000 million per cc. (2.5 cc., 10 cc., 25 cc.)

PERTUSSIS VACCINE, ALUM PRECIPITATED, U. S. P. (at least 10,000 million killed H. pertussis phase I per cc.). Should be given as early as 2 to 3 months of age or any time thereafter.

Dosage. Three 0.5 cc. at intervals of 1 month for total dose of 25,000-40,000 million. (See Immunization Schedule.)

Dosage form. *Ampuls*, 30,000 million per cc. (0.5 cc., 1.5 cc., 6 cc.).

PLAGUE VACCINE, N. F. Each cc. contains at least 2,000 million killed plague bacilli, selected for high antigenic efficiency, in a sterile suspension. Used for the prevention of plague, but the degree of protection afforded by vaccination is, as yet, incompletely assessed.

Dosage. 0.5 cc. and 1 cc. subcutaneously with a 7- to 10-day interval. Children below 10 years of age, one-half of the adult dosage. Infants under 1 year, two doses of 0.25 cc. each. Whenever the risk is great, repeated inoculations should be made at monthly intervals.

Dosage forms. *Ampuls*, 2 cc., 20 cc.

RABIES VACCINE, U. S. P. (Semple method). Consists of killed (phenolized) fixed rabies virus in 20% rabbit brain suspension.

Dosage. Usually one container (0.5 cc.) daily for 14 to 21 days injected subcutaneously into the abdominal wall.

Indications. Immunization is indicated following a bite or exposure to the saliva of an animal showing signs of rabies, when the animal responsible cannot be examined. Otherwise the animal should be observed for rabies for 14 days under a veterinarian's care.

Complications. Acute myelitis with paralysis is a rare but serious complication occurring 1 to 4 weeks after the start of vaccination.

Dosage form. Packages of 7 or 14 ampuls.

ROCKY MOUNTAIN SPOTTED FEVER VACCINE, N. N. R. Prepared from membranes of embryonated chicken eggs infected with Rickettsia rickettsii. It is used in the prevention of Rocky Mountain spotted fever by leading to the development of an active immunity. Where exposure is likely, vaccination is recommended yearly.

Dosage. Three subcutaneous injections of 1 cc. each; 7 to 10 days between injections. For children under 12 years of age, 3 injections of 0.5 cc. 7 to 10 days apart. Infants under 1 year, 3 doses of 0.25 cc. each. A booster dose of 1 cc. for adults, and 0.5 cc. for children under 12 is recommended yearly.

the entire contents of a tube is used. Each person ... reactions will result from the "vaccination": "take," "accelerated reaction," or "immune reaction." (See Immunization Schedule, for dosage.)

Precautions. Chief danger is infection such as erysipelas, other coccoid infections, or, rarely, tetanus. The vaccinated person should not touch the lesion. Shields should not be used. Post-vaccinial encephalitis is a rare complication. Eczema, open skin lesion, active tuberculosis are generally considered contraindications to routine vaccinations.

Dosage forms. *Capillary tubes* in packages of 1, 5, and 10 tubes.

TYPHOID AND PARATYPHOID VACCINES, U. S. P. Suspension of killed typhoid bacilli (Salmonella typhosa) 1,000,000,000 organisms per cc.; killed paratyphoid "A" bacilli (Salmonella paratyphii) and killed paratyphoid "B" bacilli (Salmonella schottmulleri) 250,000,000 each. Used for prophylaxis against typhoid and/or paratyphoid fevers. May also be used in foreign protein therapy. It should be noted that prophylactic vaccination is not a substitute for the control of sanitary conditions.

Dosage. Immunization—Three injections, subcutaneously, of 0.5 cc. each at 7- to 10-day intervals. A stimulation injection of 0.5 cc. subcutaneously or 0.1 cc. intradermally is recommended yearly. Children below 5 years, half dose. For foreign protein therapy the vaccine is given intravenously in small doses and increased daily or every other day. The initial dose is usually 0.1 cc. as a test dose.

TYPHUS VACCINE, EPIDEMIC, U. S. P. Made from chick yolk-sac cultures of epidemic typhus rickettsiae. It is used to produce active immunity against epidemic typhus (*R. prowazeki*: louse-borne).

Dosage. Two injections of 1 cc. each, subcutaneously, with a 7- to 10-day interval between injections. Booster immunization dose is 1 cc. every 6 months. Children under 10 years of age, one-half the adult dosage. Infants under 1 year, 3 doses of 0.25 cc. each.

Caution. Persons who are known to be allergic to egg, chicken, or chicken feathers may react unfavorably.

Dosage form. Ampuls, 20 cc.

YELLOW FEVER VACCINE, U. S. P. This is a live culture of modified yellow fever virus, which, while no longer producing yellow fever, retains its power to stimulate antibody production. It should be stored continuously at near freezing temperature, and after dilution must be used within 1 hour. Revaccination should be at least every 4 years.

Dosage. Adults and children: single dose of 0.5 cc. subcutaneously.

Dosage forms. Ampuls, powder, for 5 doses, 20 doses, and 100 doses.

TOXOIDS

DIPHTHERIA TOXOID, U. S. P. (Diphtheria Toxoid Fluid). For active immunization against diphtheria. (See Immunization Procedures, p. 130.)

Dosage. Three 0.5 cc. doses intramuscularly at intervals of 3 to 4 weeks. Booster dose 0.25 to 0.5 cc. at age of 2 years and before entering school. The use of fluid toxoid is preferable for toxoid-sensitive persons, since reactions are less severe than those to alum precipitated toxoid. (See sensitivity test under Diphtheria Toxoid, Alum Precipitated, p. 129.)

Dosage for *Ampuls* 1 cc., 1.5 cc., 7.5 cc., 22.5 cc., 30 cc.

the precipitate obtained by heating alum under various conditions in toxoid. Alum precipitated toxoid is a somewhat better antigen because of the local stimulating effect of the alum on the tissue.

Dosage. Two 0.5 cc. doses intramuscularly at an interval of 1 month. Mild to severe unpleasant reactions and occasional sterile abscess formation may be encountered with alum precipitated toxoid. For convenience the toxoid may be combined with whooping cough vaccine and tetanus toxoid. (See Immunization Procedures, p. 130.)

Precaution in the use of diphtheria toxoid. For adults, and for older children upon entering secondary school, a Schick test (p. 124) should be done. Negative and pseudo reactors require no further immunization (the test itself having served as a small booster). Positive reactors should be given a toxoid sensitivity test consisting of 0.1 cc. of 1:100 dilution of toxoid (intracutaneously). If after 48 hours the local reaction produced exceeds 1 cm. in diameter, the first injection of the undiluted toxoid should not exceed 0.1 cc. Otherwise, the recommended dosage of toxoid is given in the usual manner.

Dosage form. *Ampuls*, 0.5 cc., 1 cc., 2.5 cc., 5 cc., 10 cc.

DIPHTHERIA TOXOID ALUM PRECIPITATED AND PERTUSSIS VACCINE COMBINED (Diphtheria toxoid alum precipitated and 25,000 million killed H. pertussis per cc.)

Dosage. Three 0.5 cc. doses at intervals of 1 month, as early as 2 to 3 months of age or any time thereafter. (See Immunization Schedule, p. 130.)

Dosage form. *Ampuls*, 30,000 million H. pertussis per cc., plus diphtheria toxoid, alum precipitated (0.5 cc., 1.5 cc., 7.5 cc.).

DIPHTHERIA AND TETANUS TOXOIDS, ALUM PRECIPITATED U. S. P.

Dosage. Two 0.5 cc. intramuscular doses at interval of 1 month or more. For basic immunization see immunization schedule below.

Dosage form. *Ampuls*, 0.5 cc., 1 cc., 2.5 cc., 5 cc., 10 cc.

DIPHTHERIA AND TETANUS TOXOID WITH PERTUSSIS VACCINE COMBINED, ALUM PRECIPITATED, N. N. R. ("DTP"), (See Immunization Schedule, p. 130.) Combination of Diphtheria and Tetanus Toxoid alum-precipitated and 10,000 million killed H. pertussis phase I, per 0.5 cc.

Dosage form. *Ampuls*, 0.5 cc., 1.5 cc., 2 cc., 2.5 cc., 5 cc., 7.5 cc., 10 cc.

STAPHYLOCOCCUS TOXOID, N. N. R. Prepared from Staph. aureus and albus. Given subcutaneously in 0.1 cc. dose (containing 10 rabbit skin necrotizing doses) weekly, if indicated by failure of other methods to control infection.

Dosage form. Set of two 5 cc. *ampuls*, one containing 100 necrotizing doses and one containing 1,000 necrotizing doses.

TETANUS TOXOID, U. S. P. (Tetanus Toxoid, "Fluid"). Indicated for booster injection after a wound, because of its rapid secondary response.

Dosage. Three 0.5 cc. doses at intervals of 3 to 4 weeks, subcutaneously or intramuscularly gives immunity in 6 to 8 weeks. Booster every 5 years.

Dosage form. *Ampuls*, 1.5 cc., 7.5 cc., 15 cc.

TETANUS TOXOID, ALUM PRECIPITATED, U. S. P. Purified precipitate obtained from standardized tetanus toxoid by the addition of aluminum and

Schedule, below). This will induce a prompt increase in the antibod
10 to 100 times the preinjection level.

Reactions to the toxoid are rare (2 in 100,000 injections). For tho
exhibiting tetanus toxoid sensitivity, the total amount is given in sm
at more frequent intervals, the series to be completed in the same long
as the routine immunization.

Dosage form. *Ampuls*, 0.5 cc., 1 cc., 2 cc., 5 cc., 10 cc.

IMMUNIZATION SCHEDULE AND PROCEDURE FOR CHI

Age	Immunizing agent
3 months	Diphtheria-tetanus toxoid, alum precipitated, combined with pertussis vaccine. (DTP) (4 doses at monthly intervals).
4 months	do
5 months	do
6 months*	do
7–12 months	Smallpox vaccination
12 months	Schick test
2–3 years	DTP booster
5–6 years	DTP booster and smallpox revaccination

*If immunization is started after 6 months of age, 3 monthly doses of DTP are sufficient.

Procedure. Alternate, lateral gluteal regions are preferred sites of in
slow absorbing antigens (alum). Syringes (1 cc.) and needles (25 gau
sterilized by dry heat one hour are preferable. Each intramuscular d
istered is terminated with 0.1 cc. of air. Massage site gently with ste

Reactions. The only local reaction of importance is the formatio
circumscribed nodule which may be palpable for 4–6 weeks. An occasio
alum abscess" may also occur. No other serious systemic reactions
transient fever and irritability have occurred in the majority of i
munized.

After exposure or injury of previously immunized individuals a boos
0.5 cc. of a single antigen (fluid) or DTP as preferred may be given.

Booster Inoculation for Older Children and Adults. (Other than g
above table.) In booster inoculations against diphtheria, tetanus, an
in older children (over 8 years), and in adults, single antigens are rec
because they produce less reaction than do multiple antigens. A Schi
toxoid sensitivity test should be done before a booster injection of
toxoid (see Diphtheria Toxoid) is given to older children or adults.

After an injury, children previously immunized against tetanus sho
a single 0.5 cc. dose of tetanus toxoid ("fluid"). Plain ("fluid") tox
more rapid response than does the alum precipitated.

Children previously immunized and exposed to whooping cough ma
a single dose of pertussis vaccine (plain).

Chapter 24.
SPASMOLYTICS

Spasmolytic drugs reduce or abolish smooth muscle spasm.[1] Some act mainly through the autonomic division of the nervous system either by *anticholinergic action* (e. g., *atropine and other belladonna alkaloids*) *or by stimulation* of the adrenergic system (e. g., ephedrine, ephedrine). Others achieve relaxation by more direct action on smooth muscles.

None of the many drugs used as spasmolytics is entirely satisfactory. Spasmolytics vary in the effectiveness of their actions according to the locus of the spasm. For example, ephedrine is more effective against bronchospasm than against ureteral colic. In some instances, a spasmolytic drug may not be dependable from patient to patient, or from time to time in the same patient. In considering the numerous drugs used as spasmolytics, the objective has been to select the best in each group.

ATROPINE AND RELATED ALKALOIDS

ATROPINE SULFATE, U. S. P. Sulfate of an alkaloid obtained from the belladonna plant. White crystalline powder, soluble 1 in 0.4 in water; freely soluble in alcohol (1:5).

Atropine acts upon the secretory and the motor activities of the systems affected by the anticholinergic division of the autonomic nervous system. Its action *is anticholinergic*. Atropine works best as a spasmolytic in the eye (action on the iris). It is somewhat effective in the gastrointestinal tract; in the respiratory tract (*fairly so in asthma*); and in the upper urinary tract.

Belladonna, its preparations, and its derivatives (other than atropine) do not appear to have significant *advantages as spasmolytics over atropine itself*. It is recommended that atropine sulfate tablets (or solution, where necessary) be used instead of Belladonna Tincture. The usual dose of the tincture ranges from 0.3 to 1 cc. The tincture is assayed for total alkaloids, calculated as hyoscyamine or atropine, but there is no constant factor or proportion of specific alkaloids. Based on total alkaloidal content one may use a rough relationship of 0.3 mg. of atropine sulfate to 1 cc. (15 minims, or *30 drops*) of tincture.

Dosage. *Gastrointestinal disorders* (colic, painful spasm due to gastric, duodenal, or intestinal ulcers, spastic constipation): *Atropine sulfate*, 0.25 mg. one-half hour before meals, increased or decreased as indicated; *Belladonna tincture*, see preceding paragraph. *Pylorospasm in infants*: Use 1:1,000 solution.[2] *Preanesthetic medication: 0.3 to 0.6 mg. to inhibit salivary and other mucous secretions. Dental procedures and oral surgery, to inhibit salivary secretion:*

[1] *The term "antispasmodic" applies to skeletal and smooth muscle.*

[2] Prescription: Atropine sulfate, 0.03 gm., distilled water, to 30.00 cc. Give one drop in one teaspoonful of water, 10 minutes before feedings. Increase one drop each successive feeding until baby has atropine flush. Continue with a dose of one drop less than amount necessary to obtain flush, before each feeding

tion is 1%, varied as indicated. A dosage schedule customarily used is 1 drop instilled in each eye three times daily for three days prior to examination, and one drop on the day of examination. For older children and adults, see homatropine hydrobromide. *Iritis:* 1% solution, 2 or 3 times daily or as needed to keep pupil dilated and ciliary body relaxed; or 1% atropine sulfate ointment. *Warning:* Increased intra-ocular pressure may develop from the use of atropine; do not use in the presence of increased pressure; discontinue if increased pressure occurs during treatment. Dark glasses should be worn to decrease photophobia.

Dosage forms.

Tablets, U. S. P., 0.66 mg., 0.25 mg., 0.3 mg., 0.4 mg., 0.6 mg.

Ointment, ophthalmic, 1%.

(*Belladonna Tincture*, see statement, p. 131.)

HOMATROPINE HYDROBROMIDE, U. S. P. Mandelic acid ester of tropine, prepared synthetically. (Atropine is the tropic acid ester of tropine.) White crystals or powder. Affected by light. Soluble 1:6 in water; 1:40 in alcohol.

Actions and uses. To produce cycloplegia. Usually preferred for older children and adults. Also for treatment of iritis.

Dosage. Cycloplegia: Concentration and administration varies among ophthalmologists. One dosage schedule in use consists of three instillations of a 5% solution with a 5-minute interval between the first and second instillation and a 10-minute interval between the second and third. Frequently this is combined with 2½% neo-synephrine solution. *Iritis:* 5% solution, 3 times daily, as indicated. See under atropine sulfate for precautions against increase of intra-ocular tension.

Dosage forms. Aqueous solution, as desired.

SCOPOLAMINE HYDROBROMIDE, U. S. P. ("Hyoscine Hydrobromide"). Hydrobromide of an alkaloid obtained chiefly from hyoscyamus and scopola. Colorless crystals, freely soluble in water (1:1.5) and soluble in alcohol (1:20).

Actions and uses. Scopolamine resembles atropine in its peripheral action but differs markedly in its central action. Scopolamine is a central depressant in all doses while moderate doses of atropine are stimulants. *The sedative effect* of scopolamine is used to give symptomatic relief in postencephalitic parkinsonism, paralysis agitans, and other spastic and rigid states. Dosage used is 0.3 mg. to 0.6 mg. 3 or 4 times daily, if there is no sensitivity to the drug. This dose may be increased to obtain relief, if tolerated.

Scopolamine is also used for its *mydriatic effect.* It is less irritating than atropine; mydriasis is somewhat briefer but onset is quicker; and intra-ocular tension is less affected. For cycloplegia a 0.2% solution usually is used; for iritis and similar conditions 0.1%.

Preanesthetic medication. 0.3 mg. to 0.6 mg.

Dosage forms. Tablets U. S. P., 0.3 mg.; 0.4 mg.; 0.6 mg.

SYNTHETIC SUBSTITUTES FOR ATROPINE. These attempt to provide the spasmolytic effects of atropine with reduced or absent side effects on the pupil, heart, and secretions. The only such agent currently having official and N. N. R. acceptance is homatropine methylbromide, which is included here.

in alcohol.

Actions and uses. In the treatment of gastrointestinal spasm, not hyperchlorhydria. In animals, it has been shown to be less active (though less toxic than atropine.

Dosage. Adults—2.5 to 5 mg. 3 times daily before meals. Children and infants—According to age.

Dosage forms. *Tablets*, 2.5 mg., 4 mg.

BARBITURATES

The barbituric acid derivatives are perhaps the most effective spasmolytics available despite the accompanying disadvantage of their hypnotic effect. (See section on Barbituric Acid Derivatives, p. 118.)

NARCOTICS

MEPERIDINE HYDROCHLORIDE, U. S. P. (Demerol Hydrochloride). See under "Analgetics", p. 33.

PAPAVERINE HYDROCHLORIDE, U. S. P. Papaverine (one of the benzylisoquinoline opium alkaloids) is effective in bronchospasm, gastrointestinal spasm, biliary colic, and spasm affecting smooth muscle in general. Also valuable in the treatment of angina. However, its chief use has been in increasing collateral circulation in peripheral or pulmonary arterial embolism. For this purpose papaverine hydrochloride is given subcutaneously in doses ranging from 30 to 100 mg.

Dosage. Usual dose: 0.1 Gm.

Dosage forms.

Injection, U. S. P., *ampuls*, 2 cc. containing 60 mg.

Tablets, U. S. P., 0.1 Gm.

NITRITES

This group *includes salts and esters of nitrous acid, and organic nitrates which* are reduced to nitrites in the body. They act directly on smooth muscle. Their chief value is in the relaxation of blood vessel tonus, their vasodilating effect being followed by prompt fall in blood pressure. The nitrites are not uniformly dependable for gastrointestinal spasm.

AMYL NITRITE, U. S. P. Onset of action is more rapid (acts within 30 seconds) and duration briefer (about 5 minutes) than the other nitrites. It is used chiefly in angina pectoris and in conditions associated with arterial spasm; also in bronchospasm.

Usual dose. 0.2 cc. by inhalation.

Dosage forms. Glass *ampuls* which are crushed in a handkerchief.

GLYCERYL TRINITRATE U. S. P. (Nitroglycerin). Onset of action is slower (1 to 2 minutes) and duration longer (about ½ hour) than that of amyl nitrite.

U. S. P. usual dose. 0.4 mg. For prevention or modification of angina pectoris or other smooth muscle spasm 0.4 mg. to 0.6 mg. sublingually, every 2 to 3 hours. For acute attacks, 0.4 mg. sublingually every 5 minutes until pain is relieved.

Dosage. 15 to 30 mg. tablet every 4 to 6 hours as needed.

Dosage forms. *Tablet* U. S. P. 15 mg., 30 mg.

SYMPATHOMIMETIC DRUGS

See ephedrine, p. 137 and ephedrine, p. 138 in chapter on "Sympathomimetic Amines."

XANTHINE DERIVATIVES

Theophylline, theobromine, and caffeine—methyl derivatives of xanthine—are the only methylxanthines of clinical importance. As spasmolytic drugs, they act principally on the coronary arteries and bronchioles. Methylxanthines produce spasmolysis by direct effect and also through central nervous system stimulation. Moderate spasmolytic effect is obtained on peripheral vessels and the biliary tract.

Theophylline is the most powerful spasmolytic of the group, followed by theobromine, and then caffeine. Tolerance develops to each of these drugs and some degree of cross-tolerance exists.

The drugs in this group are irritating and therefore should be given after meals. The gastric tolerance frequently limits the dosage. Enteric coated tablets are used to avoid gastric irritation.

AMINOPHYLLINE, U. S. P. (theophylline ethylenediamine).

Dosage. U. S. P. usual dose: Oral, 0.2 Gm.

Oral doses of 0.1 Gm. to 0.2 Gm. may be given three times daily, as tolerated. Intravenous dose, 0.25 Gm. to 0.5 Gm. in 10 cc. isotonic sodium chloride solution, given slowly. For intramuscular use, 0.5 Gm. in 2 cc.

Dosage forms.

Tablets, U. S. P., enteric coated: 0.1 Gm., 0.2 Gm.

Injection, U. S. P.: *Ampuls* (pH less than 8.5 to avoid tissue damage) Intramuscular, 0.5 Gm. in 2 cc.; Intravenous, 0.25 Gm. in 10 cc.

Suppositories, U. S. P., 0.5 Gm.

THEOBROMINE CALCIUM SALICYLATE, U. S. P.

Dosage. 0.5 Gm. to 1 Gm. three times daily after meals.

Dosage forms. *Tablets*, U. S. P. enteric coated, 0.5 Gm.

Caffeine is not recommended for spasmolysis because of its pronounced stimulating effect on the central nervous system.

Chapter 25.

RESPIRATORY STIMULANTS

DIRECT STIMULANTS

CAFFEINE AND SODIUM BENZOATE, U. S. P. Mixture of equal parts of caffeine and of sodium benzoate, soluble 1 in 1.2 parts of water.

Actions and uses. Caffeine and Sodium Benzoate is a moderately efficient central nervous system stimulant whose use is limited to the treatment of moderately severe depression states such as alcoholic intoxication, mild barbiturate or opiate poisoning and similar depressive states where the patient is conscious but judgment is poor and behavior disorganized.

Dosage. 0.5 to 1 Gm. intramuscularly, to counteract poisoning by depressants.

Dosage form. Caffeine and Sodium Benzoate Injection, U. S. P., ampuls, 0.5 Gm. in 2 cc.

CARBON DIOXIDE, U. S. P. Colorless and odorless gas; 1 volume soluble in about 1 volume of water.

Actions and uses. Carbon dioxide, in concentrations less than 7% is one of the best respiratory stimulants. It is usually given in a mixture of 5% carbon dioxide with 95% of oxygen. It is particularly useful in carbon monoxide poisoning. Carbon dioxide would seem to be of doubtful value in resuscitation of patients whose blood CO_2 content is already high.

Carbon dioxide is also very useful in combating and preventing atelectasis following operative anesthesia (particularly other anesthesia) and excessive depression from thiopental anesthesia.

The gas should not be given for prolonged periods, usually not more than 30 minutes and preferably only for 5 to 15 minutes at a time. Use with caution if respiratory obstruction is present. Intoxication signs are marked dyspnea, rise of blood pressure, nausea, and vomiting.

Solidified carbon dioxide ("dry ice", "carbon dioxide snow") is used as a cauterizing agent for the removal of warts and superficial growths.

PENTYLENETETRAZOL, U. S. P. (Metrazol) (Pentamethylenotetrazol.) White crystals readily soluble in water and most organic solvents.

Actions and uses. Stimulates the mid-brain, the medullary centers, and possibly the spinal cord. High dosage produces epileptiform convulsions. Stimulates respiration and raises the blood pressure (after preliminary fall) when given in convulsive doses. The stimulating effect on the medulla is more prominent when this area is depressed than when it is functioning normally. Heart and peripheral blood vessel action is negligible. Moderate doses produce a fall in blood pressure.

Pentylenotetrazol is useful in the treatment of poisoning by central nervous system depressants (particularly barbiturates), but it is less effective than picrotoxin. It is also use[illegible] in the co[illegible]ulsion treatment of schizophrenia.

Dosage. 0.1 to 0.3 Gm. by mouth or intravenously (1 to 3 cc. of 10% solution).

Dosage form. Metrazol *Ampuls*, 1 cc. and 3 cc., containing 0.1 Gm. per cc.

PICROTOXIN, U. S. P. Glycoside obtained from the seeds of *Cocculus indicus*, a plant indigenous to Malabar, Ceylon, and other parts of Asia. It is slightly soluble in water (1 in 350); stable in air but affected by light.

Actions and uses. This convulsive poison, when used in appropriate doses and under close supervision, is a good clinical antidote for acute, profound poisoning by barbiturates and other hypnotics. The therapeutic objective is to limit its stimulant effect to those depressed medullary and mid-brain centers controlling vital autonomic functions. To accomplish this, picrotoxin is administered intravenously to the moribund patient in minute amounts (1 to 10 mg.) at intervals of 1 to 30 minutes depending on the depth of the narcosis and the observed responses to the drug. In a sense, this clinical procedure may be likened to chemical titration in that the depressant effects of the hypnotic are neutralized by the stimulant effects of picrotoxin; the desired end point being the return *and* maintenance of depressed respiration, reflexes, sensorium, etc., to *nearly* normal levels. Each patient represents an individual problem since data on dosage, tolerance, and other factors are rarely obtainable. Overdosage with picrotoxin is heralded by muscular twitching and may be corrected with Thiopental Sodium (Pentothal Sodium), 0.1 to 0.2 Gm. intravenously.

See also *Amphetamine Sulfate*, for the treatment of barbiturate and other hypnotic poisoning.

Dosage form. Picrotoxin *Injection* U. S. P., *ampul*, 20 cc. containing 3 mg. per cc. (0.3%).

REFLEX STIMULANTS

AMMONIA. This is a volatile irritant which, on inhalation, acts as a reflex vasoconstrictor and restores circulation in syncope. It is inhaled in the form of Aromatic Ammonia Spirit, U. S. P., a hydro-alcoholic solution of ammonia-yielding compounds, flavored with lemon oil.

Dosage forms. *Aromatic* Ammonia *Spirit*, U. S. P.; Aromatic Ammonia *Ampuls*, for inhalation.

Chapter 26.

SYMPATHOMIMETIC AMINES

The sympathomimetic amines produce effects identical with stimulation of the sympathetic nervous system. They are used for hemostasis, pupillary dilatation, vasoconstriction, cardiac stimulation, bronchial dilatation, etc.

FOR BRIEF EFFECT

EPINEPHRINE, U. S. P.

a. *Systemic use.* *Anaphylactic, nitritoid, and like conditions; bronchial asthma; cardiac asthma; cardiac or circulatory failure; heart block with syncope: 1:1000 solution,* 0.1 cc. to 0.6 cc. subcutaneously or intramuscularly. *1: 1000 solution, diluted to 1:100,000,* 0.05 cc. to 0.2 cc. slowly intravenously. *1:500 suspension of epinephrine in oil,* 0.5 cc. to 1.5 cc. intramuscularly. *1:100 aqueous solution,* 1 to 2 cc. for oral inhalation for 3 to 10 minutes through special all-glass atomizer.

Dose for children. Approximately one-half the above.

b. *Local use.* *Superficial bleeding:* 1:10,000 to 1:1,000 solution applied to bleeding surface. *With local anesthetics:* Concentration of 1:50,000.

Dosage forms.

Epinephrine Solution U. S. P., 1:1,000 aqueous solution of epinephrine rendered soluble with hydrochloric acid. The solution, if undiluted and aseptic, is fairly stable. It is intended for local use. Diluted solutions oxidize in a few hours, changing to a pink and gradually to a brown color. (See "Epinephrine Injection" for parenteral use.). *Dispensed in light-resistant,* 30 cc. bottles.

Epinephrine Injection, U. S. P.: 1:1000 sterile epinephrine solution, for parenteral use. In 1-cc., 10-cc., 30-cc. ampuls.

Epinephrine in Oil Injection, U. S. P.: 1:500 in vegetable oil, for intramuscular injection. In 1-cc. ampuls.

Epinephrine Inhalation, U. S. P.: 1:100 in isotonic sodium chloride solution, for oral inhalation. In 5-cc. bottles.

PHENYLEPHRINE HYDROCHLORIDE, U. S. P. (Neo-Synephrine Hydrochloride).

a. *Systemic use.* Its action is similar to that of epinephrine, with less effect on the heart. It is much more stable than epinephrine and in contrast to it, may be taken orally, to produce a vasopressor effect.

In patients receiving spinal anesthesia, to combat acute hypotension: 0.1 cc. to 1 cc. of 1% solution *subcutaneously or intramuscularly, initial dose not exceeding* 0.5 cc. and at intervals of not less than 10 minutes for subsequent doses. Superior to ephedrine for this purpose as it has no central nervous system effect.

b. *Local use.*[1]

[1] For nasal use, vehicle should not be oil. Frequent use of nasal decongestants results in "rebound"

synechiae: 1 drop of 10% solution or emulsion, preceded by local anesthetic.

Surgical and dental anesthesia, to prolong the effect of local anesthetics: 0.3 cc. to 0.5 cc. of 1% solution, per 10 cc. of local anesthetic solution.

Dosage forms.

Solution, 1%, parenteral use, in 1-cc. and 5-cc. ampuls.

Solution, 0.25%, for local use.

Solution, ⅛%, 2½% in 15 cc. bottles; 10% in 4 cc. bottles for eye.

Emulsion, 1%, 15 cc.; 10%, 3 cc., for eye.

Jelly, 0.5%, for nasal use, ⅝ oz. and 1½ oz. tubes.

NORDEFRIN (COHEFRIN) HYDROCHLORIDE, A. D. R. For dental use only at this time, in combination with local anesthetics. The following combination usually is used: Procaine HCl, 2%; Tetracaine (Pontocaine) HCl, 0.15%; Cohefrin HCl, 1:10,000. (See "Agents Used in Dental Practice," p. 67).

FOR PROLONGED EFFECT

EPHEDRINE SULFATE, U. S. P. This is the salt of levorotatory ephedrine (l-ephedrine). Its action is much longer than epinephrine and it is a potent stimulator of the central nervous system.

a. *Systemic use. Chronic hypotensive states; hypotension in spinal anesthesia; heart block with syncope; bronchial asthma; hay fever, etc.; poisoning by morphine, barbiturates and other central depressants* (see also picrotoxin and amphetamine); *narcolepsy and catalepsy* (see also amphetamine):

25 mg. to 50 mg. orally, repeated 2 to 4 times daily.

25 mg. to 50 mg. subcutaneously.

U. S. P. usual dose: 25 mg.

In heart block with syncope, avoid larger doses than necessary. In continued use, such as for bronchial asthma, sedative may be necessary to overcome irritability. Injection to combat hypotension in spinal anesthesia usually is made 30 to 45 minutes before injection of anesthetic, then repeated as needed.

b. *Local use.*[3] *Nasal decongestant:* 1 to 2% aqueous sol. made isotonic with sodium chloride and preserved with chlorobutanol, 0.5%

Dosage forms.

Ephedrine Sulfate Capsules, U. S. P., 25 mg., 50 mg.

Ephedrine Sulfate Solution, 1% with sodium chloride and chlorobutanol.

Ephedrine Sulfate Injection, U. S. P., ampuls, 1 cc. containing 50 mg. (¾ gr.).

AMPHETAMINE SULFATE, U. S. P. Racemic Amphetamine Sulfate.

Actions and uses:

Narcolepsy, mild depressive states, and for the temporary management of migraine: small initial dose to determine individual tolerance, 5 mg. or less; gradually increase until desired effect, up to 40 mg. per day. To avoid insomnia do not give in evening.

Postencephalitic Parkinson's disease: 10 to 20 mg. before breakfast and again at noon with 2.5 to 4 mg. atropine sulfate 3 times daily.

[3] See footnote, p. 137.

Dosage for Rx. Tablets U. S. P., 2 mg., 5 mg. (scored in quarters), ampuls, 20 mg. in 1 cc.

NAPHAZOLINE HYDROCHLORIDE, U. S. P. (Privine Hydrochloride.)

Nasal decongestant. Privine Hydrochloride Solution. (Mild Naphazoline Hydrochloride Solution), 0.05%, for all ordinary use. (Solution is buffered to pH of 6.2 to 6.3 with exsiccated sodium phosphate, sodium chloride, potassium chloride, and potassium biphosphate, and preserved with sodium ethyl-mercuri-thiosalicylate, 1:100,000.)

Dosage forms. *Solution:*

0.05% (Mild Naphazoline Hydrochloride Solution, U. S. P.).

0.1% (Strong Naphazoline Hydrochloride Solution, U. S. P.).

VITAMINS

These substances, the common source of which is in the diet, are essential to health. Storage in the body varies with each vitamin, but in general is not very good. Hence, they are needed regularly in effective amounts. In theory, vitamin fortification of the diet should be unnecessary. In practice, however, it is indicated for persons whose diet is inadequate.

Ordinarily, for individuals having proper nutritional balance, nothing is gained by vitamin fortification nor by furnishing amounts in excess of basic needs. With some (e. g. vitamin D), harm may result from overdosage.

The selection of vitamins and vitamin preparations has been limited to those which have established themselves in the prevention and treatment of deficiency states.

Until such time as the use of the following vitamins rests on a sound therapeutic basis, they will not be included: pantothenic acid, pyridoxine, Vitamin E.

The daily dietary allowances (desirable intake) for the vitamins, as set forth by the Food and Nutrition Board of the National Research Council, are as follows:

	Vitamin A, I. U.	Thiamine HCl, mg.	Ribo-flavin, mg.	Nicotina-mide, mg.	Ascorbic acid, mg.	Vitamin D, I. U.
Men						
Sedentary	5,000	1.2	1.8	12	75	
Physically active	5,000	1.5	1.8	15	75	
Heavy work	6,000	1.8	1.8	18	75	
Women						
Sedentary	5,000	1.0	1.5	10	70	
Moderately active	5,000	1.2	1.5	12	70	
Very active	5,000	1.5	1.5	15	70	
Pregnancy (latter half)	6,000	1.5	2.5	15	100	400
Lactation	8,000	1.5	3.0	15	150	400
Children up to 18 years						
Under 1 year	1,500	.4	.6	4	30	400
1-3	2,000	.6	.6	6	35	400
4-6	2,500	.8	1.2	8	50	400
7-9	3,500	1.0	1.5	10	60	400
10-12	4,500	1.2	1.8	12	75	400
Children over 18 years						
Girls:						
13-15	5,000	1.3	2.0	13	80	400
16-20	5,000	1.2	1.8	12	80	400
Boys:						
13-15	5,000	1.5	2.0	15	90	400
16-20	6,000	1.7	2.5	17	100	400

VITAMIN A (OLEOVITAMIN A, U. S. P.)

A primary alcohol of the benzene series, vitamin A is formed in the liver from carotene (provitamin A). Vitamin A as such is present in fish liver oils (along with vitamin D). Now also produced synthetically.

treatment of the specific deficiency state. Toxic effects from overdosage recently have been reported. Has no known local action.

Manifestations of vitamin A deficiency are:

(a) *Night blindness*—Vitamin A is essential to regeneration of visual purple.

(b) *Keratinization*—Deficiency of vitamin A results in atrophy of epithelium and replacement by stratified keratinized epithelium arising from the basal layers of the skin and mucous membranes. This metaplasia occurs in the trachea, bronchi, renal pelves, cornea, conjunctivae, tongue, and mouth. Keratinization lowers resistance to infection.

Dosage. 25,000 units of Vitamin A daily leads to rapid recovery. Daily requirement (see table of dietary allowances) to prevent deficiency is 5,000 to 8,000 units (0.6 microgram of beta carotene = 1 unit). Fortification of the average diet usually is unnecessary.

Dosage forms.

Oleovitamin A *Capsules*, U. S. P., 5,000 units, 25,000 units.

Concentrated Oleovitamin A and D, U. S. P., 60,000 units vitamin A and 10,000 units vitamin D per gram (approx. 6,000 units vitamin A and 1,000 units vitamin D in 5 drops).

Concentrated Oleovitamin A and D capsules, U. S. P., 5,000 units vitamin A and 1,000 units vitamin D.

Hexavitamin *Tablets*, U. S. P. Vitamin A, 5,000 units; vitamin D 400 units; plus 75 mg. ascorbic acid, 2 mg. thiamine hydrochloride, 3 mg. riboflavin, nicotinamide, 20 mg.

There are available *water soluble vitamin A preparations* consisting of a vitamin A concentrate dispersed in water by means of a suitable agent. The preparation listed in the N. N. R. is Aquasol Vitamin A Drops, containing 50,000 U. S. P. units per cc. Capsules are also available containing 25,000 units, and 50,000 units. These preparations have been reported to be more completely assimilated than the oil concentrate. With respect to the suspending agent, (sorbitans and others) used in these preparations, definite knowledge is not available as to the effect of long-term ingestion of the water soluble vitamin preparations in which they appear.

VITAMIN D

SYNTHETIC OLEOVITAMIN D, U. S. P. Solution of calciferol (vitamin D_2) or of activated 7-dehydrocholesterol (vitamin D_3) in vegetable oil. Vitamin D_3 is the form found in fish liver oil.

Chemical differences have been established among various D vitamins but no significant pharmacologic differences have been demonstrated.

Actions and uses. Vitamin D serves a function in the proper utilization of calcium and phosphorus. Level of the serum calcium is raised, partly by mobilization of calcium from the bones, and partly by increased absorption of calcium.

Specific in the prevention and treatment of those conditions manifested by calcium deficiency, such as infantile rickets, spasmophilia, and osteomalacia. During acute infections, especially of the gastrointestinal tract, vitamin D may be poorly absorbed. Vitamin D is also used to correct hypocalcemia or parathyroid tetany.

Vitamin D is widely used in pregnancy to help the mother meet the increased demand for calcium by the fetus.

Clinical evidence does not warrant the use of massive doses of
chronic arthritis, allergy disorders, or psoriasis. No satisfactory
been shown for any special effectiveness of vitamin A and D oin
treatment of burns, ulcers, and other lesions.

Toxicity. No tolerance to vitamin D is developed, therefore
acute or chronic, may result in abnormally high serum calcium lev
be deleterious to health, and even fatal. Therefore, the use of
should be restricted to those conditions presenting clear clinical indi

Dosage. Daily intake of 400 units is believed to meet ordinary
ment regardless of age. *For the average case of rickets*, 1,200 to 1,50
appears to suffice. In *refractory rickets*, massive doses are given, a
examined periodically for calcium casts. *Parathyroid disease*—usu
to 1,600,000 units, especially for acute parathyroid tetany. Smaller
doses must be determined individually.

Dosage forms. Synthetic Oleovitamin D, U. S. P.—May be eith
ergosterol (Vitamin D_2 or Viosterol, or Calciferol) in oil, or activa
drocholesterol (Vitamin D_3) in oil. Each 5 drops (approx. 0.1 cc. or
contains approx. 1,000 units. In various size bottles (5, 10, 20, 50,
Concentrated Oleovitamin A and D, U. S. P. (approx. 6,000 units
1,000 units Vitamin D in 5 drops).

Concentrated Oleovitamin A and D, U. S. P. Capsules (5,000 A and
Hexavitamin Tablets, U. S. P. (5,000 A and 400 D together with as
75 mg., thiamine hydrochloride, 2 mg., riboflavin, 8 mg., nicotinami

ASCORBIC ACID (VITAMIN C)

ASCORBIC ACID, U. S. P. White or slightly yellow powder.
darkens on exposure to light. In solution it rapidly deteriorates i
ence of air. Soluble 1 : 3 in water; 1 : 30 in alcohol.

Actions and uses. Deficiency may produce symptoms of scurv
said to result from inability of mesenchymal supporting tissues to form a
their characteristic intercellular substance (collagen of fibrous tissue
dentine, bone, cartilage, and the vascular endothelium are involved).

Used in the prevention and treatment of scurvy. The presence of
disease, gingivitis, gingival infection, anorexia, anemia are not in the
dicative of ascorbic acid deficiency, but may be associated with it.

Dosage. See table in introduction to Vitamins, for daily dietary
Administration of ascorbic acid: 10 mg. daily as protective dose f
therapeutic, 30 to 50 mg. Adults, 30 to 50 mg. daily, protective; 100
daily, therapeutic. Fresh orange juice: about 50 mg. per 100 cc.

Dosage forms.

Ascorbic Acid *tablets*, U. S. P., 25, 50, 100 mg.
Hexavitamin *Tablets* (includes 75 mg. ascorbic acid).
Sodium Ascorbate *Injection*, U. S. P., ampuls, 2 cc. (100 mg.),
mg.), 5 cc. (500 mg.), 10 cc. (500 mg.), 5 cc. (1 Gm.).

B COMPLEX VITAMINS

These are treated as a group because pure deficiency states to individual
of the B complex are unusual. These water soluble vitamins are es
proper nutrition. Their physiological effects are due to their essen
one or more systems having to do with

deficiency diseases, and optimum therapeutic doses.

Vitamin	Daily requirement	Deficiency disease	Optimum therapeutic daily dose
Thiamine Hydrochloride	0.4-1.8 mg. (See introductory table)	Beriberi	10 mg.
Nicotinamide (Niacinamide)	4-18 mg. (See introductory table)	Pellagra	150 mg.
Riboflavin	0.6-3 mg. (See introductory table)	Cheilosis	10 mg.

Prevention of the deficiency states. The fortification of the American diet by the addition of the B complex to bread has largely overcome the previously common deficiency in our intake. However, *individual* basic needs increase with metabolism, carbohydrate content of the diet, activity, age, and acute and chronic illnesses.

Treatment. The major consideration in treatment is an awareness that the *overt* deficiency state is probably not a pure entity; hence, in addition to its relief by specific therapy, the other members of the B complex should be given. Intramuscular or intravenous injection of 100 mg. doses of thiamine hydrochloride should only be given slowly and cautiously as severe anaphylactic-like reactions, shock, and death have been reported.

(Folic acid and Vitamin B_{12}: See "Hematics.")

Dosage forms.

(1) **Nicotinamide:** *Nicotinamide Tablets, U. S. P.*, 25 mg., 50 mg., 100 mg. *Nicotinamide Injection, U. S. P.*, ampuls, 50 mg., 100 mg. per cc., in various sizes. *Triasyn B Tablets, U. S. P.*, containing 20 mg. of nicotinamide, together with 2 mg. thiamine hydrochloride and 3 mg. *riboflavin. Hexavitamin Tablets* (see under Multiple Vitamin Therapy, p. 144).

(2) **Riboflavin** (equally effective orally or parenterally): *Riboflavin Tablets, U. S. P.*, 1 mg., 5 mg. *Triasyn B Tablets* (see above, under nicotinamide). *Hexavitamin Tablets* (see under Multiple Vitamin Therapy, p. 144).

(3) **Thiamine Hydrochloride:** *Thiamine HCl Tablets, U. S. P.*, 1 mg., 5 mg., 10 mg., 50 mg. *Thiamine HCl Injection, U. S. P.*, ampuls, 10, 100, 250, 500, 1 Gm. per cc., various sizes. *Triasyn B Tablets* (see above, under Nicotinamide). *Hexavitamin Tablets* (see under Multiple Vitamin Therapy, p. 144).

(4) **Vitamin B Complex:** *Triasyn B Tablets, U. S. P.*, 2 mg. thiamine hydrochloride, 3 mg. riboflavin, 20 mg. nicotinamide. *Vitamin B Complex Liquid*, any preparation allowing administration on the basis of 2 mg. thiamine, 3 mg. riboflavin, and 20 mg. nicotinamide per dose. Intended for convenience in pediatric practice. *Vitamin B Complex, Injectable* (nonofficial). Preparation averaging 10 mg. thiamine hydrochloride, 150–200 mg. nicotinamide and 5–10 mg. riboflavin per dose. Available in ampuls in powder form and in solution. Used to expedite *therapeutic* response especially where there may be interference with gastrointestinal absorption.

VITAMIN K

Vitamin K is necessary for the formation of prothrombin by the liver. Vitamin K is a generic term applied to certain naphthoquinone derivatives. Vitamins K_1 2-methyl-3-phytyl-1 4-naphthoquinone) and Vitamin K_2, oil soluble, are

counteract hypoprothrombinemia induced by bishydroxycoumarin (d

Actions and uses. (1) Primary vitamin K deficiency (rare). (2) He states associated with obstructive jaundice, primary hepatic disease, intestinal absorption (as in sprue, celiac disease, ulcerative colitis). (logic hypoprothrombinemia of the newborn (for prevention of resulti rhage, vitamin K may be given to the mother in labor or to the newbo (4) To counteract effect of bishydroxycoumarin (dicumarol).

MENADIONE SODIUM BISULFITE, U. S. P. Sodium bisulfite of menadione (2-methyl-1, 4-naphthoquinone.) White, odorless, h powder. Soluble 1:2 in water.

Action and uses. See Introduction above.

Dosage. 3.84 mg. (equiv. to 2 mg. menadione) daily, orally. For r low hypoprothrombinemia, especially during bishydroxycoumarin ti to 100 mg. intravenously, slowly; for dangerously low level, see Vita

Dosage forms. Menadione Sodium Bisulfite *Tablets*, 5 mg.

Menadione Sodium Bisulfite *Injection*, U. S. P., ampuls, 1 cc., 3.84 r menadione); 10 cc., 72 mg. (72 mg. menadione, 27.5 mg. sodium bisulf

VITAMIN K_1, N. N. R. (2-Methyl-3-Phytyl-1, 4-Naphthoquinone.) from natural sources or prepared from 2-methyl-1, 4-naphthoquino dione).

Dosage. If, during treatment with bishydroxycoumarin (dicum prothrombin activity drops to a dangerously low level or if signs o appear, give 1 Gm vitamin K_1 intravenously, in emulsion form. (S

Dosage form. Ampuls, 1 Gm., 5 Gm.

Multiple Vitamin Therapy

Multiple vitamin preparations are included for the prophylaxis and of conditions resulting from deficiency of Vitamin A, Vitamin D, asc thiamine, riboflavin, and nicotinic acid. For this purpose, Hexavita lets, U. S. P. are included. For convenience in administering multipl to infants and children who are unable to take tablets, liquid conce available. Those having potencies closely related to normal require to be preferred.

Multiple vitamin preparations containing folic acid should be a cause of the possibility of "masking" early pernicious anemia and thus it to become far advanced before it is recognized clinically.

HEXAVITAMIN TABLETS, U. S. P. Vitamin A, 5,000 units; Vita units; ascorbic acid, 75 mg.; thiamine hydrochloride, 2 mg.; riboflav nicotinamide, 20 mg.

Appendix

FORMATION OF MEDICAL-
ARMACEUTICAL INTEREST

VEHICLE SUGGESTIONS

ble Medications:

Vehicle	Suggested for
, U. S. P.	*Chloral Hydrate*
), U. S. P.	*Ammonium Chloride*
rup, N. F.	*Sodium Salicylate, Ammonium Chloride.*
, U. S. P.	*General use*
p, U. S. P.	*Choline Chloride,*** Potassium Iodide.*
p,* U. S. P.	*Ammonium bromide****
yrup, U. S. P.	*Diluted Hydrochloric Acid*
Syrup, U. S. P.	*Cough and cold prescriptions (slightly alkaline)*
Syrup, U. S. P.**	*Cough and cold prescriptions*
iodictyon Syrup, N. F.	*Choline Chloride,*** Quinine Bisulfate, Chloral Hydrate, Codeine Sulfate or Phosphate*

oholic Soluble Medications:

Vehicle	Remarks
ixir, U. S. P.	*Time tested vehicle*
Elixir, N. F.	*For bitter-salty substances*
Elixir, N. F.	*Pharmacist adjusts "Low" and "High" Alcoholic elixirs to correct strength required by prescription.*

lkaline carbonates (CO_2 formed)
e of many alkaloids.
ug."

Abbreviation	Latin	English
aa	ana	of each
a. c.	ante cibum	before meals
b. i. d	bis in die	twice a day
Cap.	Capiat	let the patient take
Caps.	Capsula	capsule
Chart.	Charta	paper (powder)
Coch. parv.	Cochleare parvum	teaspoonful
Collyr.	Collyrium	eyewash
Cong.	Congius	gallon
E. M. P.	Ex modo praescripto	as directed
Ft.	fiat	make
gtt.	guttae	drops
h. d.	hora decubitus	at the hour of going t
h. s.	hora somni	at bedtime
M.	Misce	mix
O.	Octarius	pint
O. D.	oculus dexter	right eye
O. L.	oculus laevus	left eye
O. S.	oculus sinister	left eye
O. U.	oculus uterque	both or each eye
p. o.	per os	by mouth
p. c.	post cibum	after meals
p. r. n.	pro re nata	as needed
q. s.	quantum sufficit	a sufficient quantity
S. O. S.	Si opus sit	if there be need
Stat.	statim	at once
ss	semis	one half
S. V. R.	Spiritus vini rectificatus	alcohol
t. i. d.	ter in die	3 times a day
Ut dict.	ut dictum	as directed

SUGGESTIONS FOR PHYSICIAN'S BAG

(*Based on 1952 usage at U. S. Public Health Service Outpatient C Washington, D. C.*)

Acetylsalicylic Acid Tablets:
- 60 mg.
- 0.3 Gm.

Alcohol, 70%

Aluminum Hydroxide Gel, Dried, Tablets, 0.3 Gm.

Aminophyllin:
- Ampuls, i.v., 0.25 Gm.–10 cc.
- Suppositories, 0.5 Gm.
- Tablets, 0.2 Gm.

Ammonia Arom. Ampuls (for inhalation), 0.333 cc.

Amyl Nitrite Ampuls (for inhalation), 0.2 cc.

HCl capsules, 50 mg. and 0.25 Gm.
Tincture
psules, 25 mg. (and/or 50 mg.)
n Chloride Tincture, U.S.P. (Zephiran)
carb. Tablets, 0.3 Gm.
Sod. Benzoate Ampuls, 0.5 Gm.–2 cc.
conate Ampuls, i.m. or i.v., 10%–10 cc.
sphate Tablets, 15 mg.
aine Ointment, 1%, Cream, ½%*
puls, 1 cc.—0.5 mg.
. Capsules, 30 mg.
lfate Capsules, 25 mg.
Tartrate:
1 mg.
0.5 mg.–1 cc.
HCl Ampuls, 1:1000–1 cc.
nitrate (Nitroglycerin) Tablets, 0.6 mg.
Jelly
HCl Ampuls, 100 mg.–2 cc.
lfate Ampins:
1 cc.
1 cc.

ocaine:
Suspension, 3 million Units
00,000 U. per cc.
ol:
15 mg.
mpuls, 0.13 Gm.
al Elixir
l, vial, 2%
ne Tablets, 60 mg.
lfate Tablets, 0.2 Gm.
Sod. Capsules, 0.1 Gm.
rbonate Tablets, 0.3 Gm.
thiazole Tablets, 0.5 Gm.
Tablets, 0.5 Gm.
Ophth. Oint., 0.5%
lled, Sterile Ampuls
lso contains adhesive tape, applicators, roll bandages, elastic bandages, otton, tongue blades, thermometers (oral and rectal), prescription nges and needles, a percussion hammer, a sphygmomanometer, a stethoscope, and a steel tape.

ng. added by station Pharmacy Committee action.

The *average dose* has been calculated to be that amount of drug that brin about the desired condition in an adult male patient weighing 150 pounds.

Bastedo's Rule

$$\frac{\text{Age in years plus 3}}{30} \times \text{Adult Dose} = \text{Child's Dose}$$

Cowling's Rule

$$\frac{\text{Age at next birthday (in years)}}{24} \times \text{Adult Dose} = \text{Child's Dose}$$

Clark's Rule

$$\frac{\text{Weight (in pounds)}}{150} \times \text{Adult Dose} = \text{Dose for Individual}$$

Fried's Rule for Infants

$$\frac{\text{Age (in months)}}{150} \times \text{the Adult Dose} = \text{the Infant's Dose}$$

Young's Rule

$$\frac{\text{Age (in years)}}{\text{Age plus 12}} \times \text{Adult Dose} = \text{Child's Dose}$$

The Code of Ethics to which professional pharmacy subscribes states in part: "Where an obvious error or omission in a prescription is detected by the pharmacist, he should protect the interest of his patron and also the reputation of the physician by conferring confidentially upon the subject, using the utmost caution and delicacy in handling such an important matter."

The pharmacist appreciates the fact that an abnormal condition may sometimes require the use of a high potency medication.

Some of the procedures and general pharmaceutical rules which are followed to substantiate the pharmacist's opinion that an *overdose* exists in a particular prescription follow. These are presented to indicate what action the pharmacist has taken before he believes it necessary that contact with the physician be established.

1. A dose double that given for the drug in the United States Pharmacopoeia or the National Formulary is generally considered to be within safe limits for adults.

2. *Children and Infant medications* are checked with such rules as Young's and Fried's. To insure this check, most physicians include the age of their patient on the prescription when this information is material. To insure proper usage of a medication, the use of "Take as Directed" in the signa should be avoided.

3. *In connection with common potent chemicals used in prescription compounding,* it is considered advisable for the pharmacist to check with the physician should certain well-established strengths be exceeded or incompatibilities be noted. For example:

DRUG CONCENTRATIONS

Mercury Bichloride, U. S. P.

A 1:500 solution is the maximum concentration normally used on the skin. A check with the physician is considered advisable beyond this strength. 1:1,000 is the usual strength prescribed.

Mercuric Chloride (Corrosive Sublimate) is offic al in the National F... in *tablet form*. Tw...

Note that the smaller tablet has been designed to produce a solution approximately one-quarter as strong as the larger tablet.

Phenol, U. S. P.

A 5 percent solution is the maximum concentration of carbolic acid normally used for ear preparations.

Potassium Permanganate, U. S. P.

An antiseptic releasing nascent oxygen. The tablet is official in the National Formulary.

For applications to the skin, a 1:2,000 solution is normally prescribed; for *irrigation purposes, a 1:15,000 to a 1:4,000* solution; for Vincent's infection, a 1% solution.

Zinc Sulfate, U. S. P.

For ophthalmic use, a one quarter of one per cent (¼%) solution is normally prescribed. Uses of 0.1% to 1% may be indicated. The usual maximum concentration is one half of one per cent solution.

Note: $ZnSO_4 \cdot 7H_2O$ is efflorescent in character. To insure an uneffloresced salt for ophthalmic prescriptions, it is purchased in as small amounts as possible and kept tightly stoppered. This insures a correct strength solution when prescribed.

Zinc Chloride, U. S. P.

A salt more astringent than the sulfate. Because of this it is used in weaker concentrations than the sulfate for ophthalmic purposes. A 0.1% solution is occasionally prescribed.

PRESCRIPTION INCOMPATIBILITIES

Bacitracin and Polymyxin in Ointment Bases

Bacitracin is unstable in aqueous preparations and in carbowax bases. Bacitracin and polymyxin diffuse slowly from the greasy base ointments. A base containing polyethylene glycol in which hydroxyl groups are esterfied appears to be the most satisfactory ointment base for these two antibiotics.

Penicillin G (Benzylpenicillin) Solutions

Aqueous solutions of crystalline salts of benzylpenicillin may be made more stable by the use of a phosphate or sodium citrate buffer. The potency of such solutions is maintained from 1 to 2 weeks. Best results are obtained when solutions are prepared using phenol and a buffer and refrigerating at about 3° C. Under these conditions, the solution appears to be stable for at least 21 days.

Penicillin Eye Drops

Recent investigations indicate that solutions containing 0.5% sodium citrate and 0.8% sodium chloride (for isotonicity) are stable for 14 days when preserved at 15° C. When indicated, penicillin eye drops should be so prepared.

Folic Acid Stability in Solution of B-Complex Vitamins

Recent studies indicate liquid preparations containing folic acid, thiamine, riboflavine, nicotinamide, pyridoxine and pantothenyl alcohol in normal quanti-

suspending agent used to keep the undissolved folic acid in suspension. Simp
syrup and propylene glycol vehicles are not desirable vehicles.

Terramycin Elixir

Any preparation added to Terramycin Elixir that alters its pH or alcohol content appreciably leads to a precipitation of the antibiotic. The pH of th combination should be below 2.6 and the alcohol content not less than 15 perce if the usual 14 day stability is desired.

Iron preparations form an Iron-Terramycin complex which precipitates slowly Aluminum Hydroxide or Kaolin preparations inactivate Terramycin. Elixir containing Folic Acid are also incompatible with Terramycin because of th differences in pH.

Iodine with Alkaloids:

Rx Iodine 30 mg.
Camphor
Menthol
Ephedrine aa 0.3 Gm.
Liq. Pot. q. s. 30 ml.
M.et Sig.: Nasal Spray

Iodine and ephedrine are incompatible. In this instance a muddy brown precipitate is produced. Iodine is incompatible with alkaloids and should not be dispensed in the same prescription. In addition, aqueous sprays, not oily, are indicated.

Carbon Dioxide Formation:

Rx Bismuth Subnitrate * 20 Gm.
Sodium Bicarbonate 10 Gm.
Peppermint water q. s. ad fl. 120 ml.
M.

Bismuth Subnitrate in the presence of water hydrolyzes to form nitric acid. The nitric acid in turn reacts with the sodium bicarbonate with the evolution of carbon dioxide gas. Several incidents of this prescription's "exploding" have been reported. By prescribing bismuth subcarbonate in place of the subnitrate this incompatibility is avoided.

Rx Potassium Citrate *
Sodium Bicarbonate
Syrup of Orange q. s. ad
M.

The vehicle, syrup of orange is acid in character due to the presence of citric acid in its formula. Acid solutions react with sodium bicarbonate forming carbon dioxide, a gas. The choice of another vehicle or the prescribing of a syrup of orange (non-acid) would overcome the incompatibility.

Acid Solutions Precipitating Phenobarbital:

Rx Phenobarbital Sodium 0.6 Gm.
Elixir of Three Bromides * q.s.ad 120 ml.
M.

Phenobarbital is precipitate by the

bromide to replace the ammonium salt will overcome the incompatibility.

Rx Phenobarbital
Syrup of Orange
Distilled water q. s.

Sodium barbital and sodium phenobarbital generally precipitate from their aqueous solutions upon the addition of an acid solution. This is due to the decomposition of the sodium salt and the separation of free barbital or phenobarbital, either being insoluble in aqueous solutions. In the above instance, the soluble or sodium salt should be prescribed (Sodium Phenobarbital) and, because the syrup of orange contains citric acid, it should first be neutralized with sodium bicarbonate, or an acid-free syrup should be prescribed, to prevent the precipitate from forming.

Ophthalmic Incompatibilities:

Rx Zinc Sulfate 60 mg.
Sodium Borate 0.6 Gm.
Dist. Water
q. s. ad 30. ml.
Sig. Eye Drops

Sodium borate is incompatible with zinc sulfate, metathesis occurring with the formation of a precipitate. By prescribing boric acid in place of the sodium borate the resulting preparation is a clear solution.

Rx Pilocarpine Hydrochloride
Mild Silver Protein Solution (5%) *
Misce.

Silver salts are precipitated from their solutions by soluble chlorides. By prescribing pilocarpine nitrate the silver chloride precipitate will not form and a clear solution will result.

THERMOMETRY FACTS

Average normal temperature of adults is 98.6° F. or 37° C. (per rectum)

Handy Rule for Comparing Thermometric Values:

Centigrade temperature plus 40, times 1.8, minus 40 equals Fahrenheit equivalent.

Fahrenheit temperature plus 40, divided by 1.8, minus 40 equals Centigrade equivalent.

Conversions

C.°	F.°
37. 0	98. 6
37. 5	99. 5
38. 0	100. 4
38. 5	101. 3
39. 0	102. 2
39. 5	103. 1
40. 0	104. 0

SOLIDS

1.000 grain	0.065 Gm. (6
15.432 grains (1 Gram)	1.00
00.000 grains (1 drachm)	3.9
437.500 grains (avoirdupois ounce)	28.35
454.600 grains (fluid ounce water)	20.57
480.000 grains (apothecary ounce)	31.10
7,000.000 grains (avoirdupois pound)	454.00

WEIGHT*

Metric	*Approximate apothecary equivalents*	*Metric*	*Approximate apothecary equivalents*
30 Gm.	1 ounce	30 mg.	½ grain
15 Gm.	4 drachms	25 mg.	⅜ grain
10 Gm.	2½ drachms	20 mg.	⅓ grain
7.5 Gm.	2 drachms	15 mg.	¼ grain
6 Gm.	90 grains	12 mg.	⅕ grain
5 Gm.	75 grains	10 mg.	⅙ grain
4 Gm.	60 grains (1 drachm)	8 mg.	⅛ grain
3 Gm.	45 grains	6 mg.	1/10 grain
2 Gm.	30 grains (½ drachm)	5 mg.	1/12 grain
1.5 Gm.	22 grains	4 mg.	1/15 grain
1 Gm.	15 grains	3 mg.	1/20 grain
0.75 Gm.	12 grains	2 mg.	1/30 grain
0.6 Gm.	10 grains	1.5 mg.	1/40 grain
0.5 Gm.	7½ grains	1.2 mg.	1/50 grain
0.4 Gm.	6 grains	1 mg.	1/60 grain
0.3 Gm.	5 grains	0.8 mg.	1/80 grain
0.25 Gm.	4 grains	0.6 mg.	1/100 grain
0.2 Gm.	3 grains	0.5 mg.	1/120 grain
0.15 Gm.	2½ grains	0.4 mg.	1/150 grain
0.12 Gm.	2 grains	0.3 mg.	1/200 grain
0.1 Gm.	1½ grains	0.25 mg.	1/250 grain
75 mg.	1¼ grains	0.2 mg.	1/300 grain
60 mg.	1 grain	0.15 mg.	1/400 grain
50 mg.	¾ grain	0.12 mg.	1/500 grain
40 mg.	⅔ grain	0.1 mg.	1/600 grain

*The above *approximate* dose equivalents have been adopted by the latest Pharmacopoeia, Nat
mulary, and New and Nonofficial Remedies, and these dose equivalents have the approval of th
Food and Drug Administration.

LIQUIDS

		Approximate values
1 minim (m)	0.061 cc	
16.23 minims	1.000 cc	
1 fluid drachm (60 m)	3.700 cc	4 cc
1 fluid ounce (480 m)	29.570 cc	30 cc
1 pint (O) (octarius)	473.000 cc	480 cc

(*Approximate Evaluations*)

Household factor	*English equivalent*	*Metric equivalent*
Drop	1 minim	0 cc
Teaspoonful	1 fluid drachm	8 cc
Dessertspoonful	2 fluid drachms	15 cc
Tablespoonful	4 fluid drachms	60 cc
Wineglassful	2 fluid ounces	120 cc
Teacupful	4 fluid ounces	240 cc
Tumblerful	8 fluid ounces	

MG. PERCENT VS. MILLIEQUIVALENTS PER LITER

To convert mg. percent readings to milliequivalent per liter, divide the milligrams per liter (1,000 cc)* by the atomic weight and multiply by the valency.** *Milligram per liter is obtained by multiplying the mg. percent by 10.

**Element	At. Wt.	Valence
Na	23	1
K	39	1
Ca	40	2
Mg	24	2
Cl	35	1
$(HPO_4)^{=}$ (mg. P)	31	1.8
$(SO_4)^{=}$ (mg. S)	32	2

FEDERAL NARCOTIC REGULATIONS*

(*Harrison Narcotic Law*)

GENERAL INFORMATION

The Physician and His Narcotic Prescriptions

1. The narcotic prescription must be written in ink or indelible pencil, or be typewritten.

2. The prescription must carry the full signature of the physician, his address and Federal narcotic registry number.

3. The prescription must include the name and address of patient, and date.

*See regulations for specific P, H, S, rules governing use of narcotics, hypnotics, alcohol and spirituous liquors.

6. Prescriptions and records must be kept on file for 2 years by the pharmacist.

NONEXEMPT NARCOTICS

(Prescription Required—Cannot be Refilled)

Cocaine, Demerol, Dilaudid, Hycodan bitartrate, Pantopon, Spasmalgin.

Note: Preparations or remedies which are within the exemption may be sold with or without prescriptions, and a prescription for such a preparation may be refilled provided, of course, the preparation is furnished in good faith for medicinal purposes only. The filling or refilling of narcotic prescriptions calling for *more than one exempt preparation* or a mixture consisting of an exempt preparation or remedy further reduced or diluted by the addition of non-narcotic medicinal agents is authorized, provided, of course, the preparation is furnished in good faith for medicinal purposes.

An extemporaneous prescription calling for narcotic *drugs* not in excess of the amounts specified in section 6 may be refilled in the same manner as a prescription calling for ready-made preparations or remedies, provided the mixture is sold in good faith for medicinal purposes only, and a record is kept of the sale in the manner indicated in Article 185. (Above regulations subject to any further restrictions imposed by the Federal *Durham-Humphrey Act* and individual *State Narcotic and Pharmacy Laws.*)

LINIMENTS, OINTMENTS AND OTHER PREPARATIONS FOR EXTERNAL USE

Regardless of the amount of narcotic content, these preparations are "exempt" narcotics, provided that they do not contain cocaine or any of its salts, derivatives or substitutes (or other nonexempt drugs such as Dilaudid, Spasmalgin, Demerol, Pantopon, Hycodan Bitartrate), and provided that these preparations contain other ingredients rendering them unfit for internal administration.

Solutions, ointments and other preparations *for use in the eye, ear or nose or for rectal, vaginal or urethral administration* are not considered as being preparations for external use.

NARCOTICS FOR OFFICE USE

Physicians may obtain for office use as much as one ounce of an aqueous or oleaginous solution of a narcotic (not exceeding 20% strength) (Article xv of Federal Harrison Act). The request must be made on the physician's official Federal Narcotic order blank and *not* on the regular prescription blank. (See rules and regulations on the inside cover of Federal Narcotic Order Book.) This order may be honored by the retail pharmacist, who shall affix a label to the package showing the date of the order; number of the order form, if any; the name and proportion of the narcotic drug contained in the solution; and the name, address, and registry number of the vendee and vendor, respectively.

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*Exempt narcotics:

The following up to:
- 2 gr. Opium
- 1 gr. Codeine
- ¼ gr. Morphine
- ½ gr. Heroin

(or their salts and derivatives**) to the fl. oz. (450 m., 30 cc.) or to avoir. (437.5 gr. 28.35 GM.) ounce (Section 6 of the Narcotic Act)

**Apomorphine—derivative of morphine (¼ gr. to oz. exempt)
Dionin (Ethyl morphine hydrochloride) (¼ gr. exemption to ounce)
Papaverine (2 gr. exemption to ounce—an alkaloid of opium)

narcotics in stock preparations, may keep, as to such preparations, in lieu of the record required by Art. 177, a record of the date when each stock preparation is made or purchased and the date when the preparation is exhausted (reb. 8, art. 179).

Practitioners' Records (Article 177)

"All persons and institutions registered in Class IV (including physicians and dentists) shall keep a daily record showing the kind and quantity of narcotics *dispensed or administered*, the *name and address of each person* to whom dispensed or administered, and the name and address of the person upon whose authority and the purpose for which dispensed or administered." In this connection, *some sort of a perpetual inventory for each item and strength carried* would seem most advisable.

Narcotics for Use by Physicians To Be Carried in Physician's Bag or for Office Use How Obtained

Narcotics, in the form of *tablets*, ampuls, and powders, may be obtained by a physician for use in his office or for carrying in his bag *only* upon the official Government order form (such as is used to order the ampoules and phenglucose *solutions*). A physician *cannot legally write a narcotic prescription* for such supplies on his regular prescription blanks. The official order form (excluding the 20% exemption referred to above) cannot be filled by a retail pharmacist. *Such orders are filled by Class 1 and 2 penalties only (such as wholesalers* and manufacturers). The order forms are prepared in duplicate, the duplicate being retained by the physician for a period of 2 years. Orders must not be written in pencil.

Fictitious Names

The law does not permit the use of a fictitious name upon a prescription.

SPECIAL TAX STAMP

Display of Narcotic Certificate

The *Special Tax Stamp* (which embodies the narcotic registration number assigned the physician and the basis of office) must be *conspicuously displayed* in the office. Federal Regulations attach penalties for nondisplay of this special tax stamp. (See art. 40.)

Special Tax Stamp—Registry Number—Prescription Blanks

Caution. In having prescription blanks printed make certain that the registry number used is *your narcotic registry number*. Violations of this regulation are constantly coming to the *attention* of the *narcotic officials*. Do not use your *State* license number, or the *special serial number* printed in *red* on the Federal special tax stamp. The registry number assigned is the number *typed* on the form, found in the body of the tax stamp and reading, "Your Registry Number Is - - - -."

Special Tax Stamp. Important—Change of Office Location

A physician's special tax stamp is valid *only* for the fixed location to which originally issued. Should a physician relocate his office, he must notify the

Office of Collector of Internal Revenue
for the district in which practice is carried on.

NARCOTIC "REFILL" PRESCRIPTIONS

Federal Narcotic Regulations forbid the use of "Refill Prescription No. ——" or similar wordings on prescription blanks. A complete new prescription must be written.

"LETTER" BY PHYSICIAN TO DISTRICT NARCOTIC OFFICE

Many physicians, for their own protection and as an indication of their good faith, file a letter with their District Narcotic Office when treating patients requiring large doses of narcotic medications over long periods of time. (Not a legal requirement.)

The letter usually states the patient's name, the condition from which the patient suffers, and a statement to the effect that it is the physician's opinion that the narcotic is indicated in treatment, that it will be used for some time, and that as the disease progresses, the dose may be unfortunately increased to sustain life and alleviate pain and suffering.

TELEPHONE NARCOTICS

Telephone prescriptions.—The furnishing of narcotics pursuant to telephone advice of practitioners is *prohibited*, whether prescriptions covering such orders are subsequently received or not. However, in an *emergency* a pharmacist may deliver narcotics through his employee or responsible agent pursuant to a telephone order, provided the employee or agent is supplied with a properly prepared prescription before delivery is made, which prescription shall be turned over to the pharmacist and filed by him as required by law (ch. 8, art. 172).

THEFTS

Physicians are requested to use due caution in protecting their narcotic drugs, order blanks, and prescription pads. Complaints have been received by the Narcotic Department of thefts of these items, especially prescription pads from offices, and physicians' professional bags stolen from unlocked autos. Notify Federal narcotic authorities at once should such thefts occur.

ANNUAL REGISTRATION

A physician intending to practice medicine and to administer or dispense narcotic drugs in the course of such practice must apply for registration under the Harrison Narcotic Law to his local Collector of Internal Revenue and must pay the necessary tax.

A physician must on or before July 1 of each year renew his Special Narcotic Tax Stamp by registering with his Collector of Internal Revenue. Special forms are supplied by the Federal Government for this purpose requesting: (1) Name of the physician, (2) Address at which practice is carried on, (3) The State professional license number and date of issue, and (4) An inventory of the narcotics on hand. (If none, mark "NONE" on inventory form.) Duplicate copy of the inventory filed must be kept by the physician for a period of 2 years. The tax

forgeries.

Don't write a narcotic prescription in lead pencil. Avoid writing any Rx pencil, many are changed to call for morphine.

Don't write for narcotics this way:

Morphine HT ¼ # X or

Morphine HT ¼ # 10

Several X's or zeros can be added to raise the amount.

Use brackets or spelling.

Don't carry a large stock of narcotics in your bag. Addicts are on the look for these in doctor's offices and cars.

Don't store your office supply where patients can get at it. Avoid storage n sink or urinal. The patient may ask to use these.

Don't fall for a good story from a stranger claiming aliment that usua requires morphine. The addict can produce bloody sputum, simulate bad cou or other symptoms. Make your own diagnosis.

Don't give a narcotic Rx to another without seeing the patient. Addicts ha posed as nurses to get doctors to prescribe narcotics.

Don't write for large quantities of narcotics unless unavoidable. Diversion addicts is a profitable business, as much as $1 for ¼ gr. M. S.

Don't prescribe narcotics on the story that another MD had been doing Consult that physician or the hospital records whenever possible.

Don't leave Rxs signed in blank at the office for nurses to fill in. Sign blanks are bad practice and many have been stolen by addicts.

"Narcotic" Don'ts," Bureau of Narcotics, Washington, D. C.

MARIHUANA REGULATIONS

MARIHUANA OR CANNABIS ACT

(*Federal*) (*1937*)

General Information

1. A special Federal permit *is required of physicians to write prescriptions fo* this drug. Physician must have a Federal Cannabis Registry number. Thi number must appear on all prescriptions for this drug and its preparations.

2. No "exempts" exist such as in Harrison Narcotic Law. Act applies to dru and its preparations.

3. Other requirements are similar to narcotic law.

4. Pharmacist must have a Cannabis Registry number to deal in this drug.

(Page numbers in bold type indicate principal points of reference.)

References in pages 6 through 28 indicate listings in the "Useful Drug List" as tabulated on those pa

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